General Principles of Therapeutics

McCRUDDEN

# A BRIEF INTRODUCTION

TO THE

# GENERAL PRINCIPLES OF THERAPEUTICS

BY

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# PREFACE

The need of an elementary text book must be apparent to anyone who has attempted to give instruction in the general principles of therapeutics. There are reference books dealing with the details of therapeutics; but there is no book which establishes a point of view regarding the many and confusing details of treatment such that these details may be contemplated, not as a vast number of empirical and unrelated elements, but as mutually dependent parts of a whole; a book that treats therapeutics as a science, as a branch of applied physiology.

The present volume is intended as a start in this direction. It is not intended as a catalogue of remedies. It can be used to supplement a practical clinical course in therapeutics, thereby eliminating some of the didactic instruction, so that the clinical instruction can be devoted entirely to illustrating (1) how the principles are actually applied, and (2) the result of treatment.

The principles are not laid down as rigidly crystallized doctrine; the purpose is not to inculcate dogma but to enlighten the understanding and to stimulate the use of the intelligence in the application of treatment. Scientific education should consist not so much in the accumulation of facts, as in the development of scientific habits of thought, in the cultivation of correct points of view; in the establishment of a state of mind in which the facts can take their proper place.

Some of the details of treatment laid down may be of doubtful value, details that further research will modify; so, too, elements of greater moment, some tenets of the principles as stated may exhibit faults and inconsistencies, or a distorted perspective in the prominence given to different parts. This is unavoidable. The details and facts must be used as the stuff to form the ideas; but they must not be taken for the idea itself. The physiological point of view outlined here may be compared with a wave; though the physical particles of which the wave is composed change from instant to instant, the wave maintains its form and character; it may be compared with life itself—with a unicellular ameba, for example; the ameba is continuously changing its form, and the particles of which it is composed are constantly changing; but the living essence, the cell itself, remains. Under the influence of a correct point of view, facts arrange themselves in order like iron filings under the influence of a magnet. The physiological point of view serves to bring system out of chaos; a statement of the facts of therapeutics subordinated to certain guiding ideas is to the disordered array of unrelated remedies and prescriptions which the student commonly accumulates, what a disciplined army is to a mob of individuals. It is simple, definite, and clear; and it is elastic enough to permit the incorporation of newly discovered elements of treatment. The chief guides in determining what principles to lay down have been *usefulness and elasticity;* the test of usefulness, to restrain any tendency toward barren abstractions; that of elasticity, to avoid the other extreme of fixed and rigid canon. As details become obsolete they can be replaced by better ones; but even though large parts of the scheme

of treatment have to be altered to conform to the results of scientific progress, the idea itself—like the ameba or wave mentioned in comparison—will still remain as a paradigm.

# INTRODUCTION.

A DISEASE may take such variable forms in different persons, and change so much from day to day in any one person, that the treatment of every new patient is a new problem. In chronic disease especially, where the exact details of treatment depend largely on the severity of the disease, on the extent to which function is disturbed, on the condition of the patient as a whole—factors concerning which exact measurements play as yet but a small part, and for which judgment is gained only by long clinical experience with cases of all grades of severity—we treat individuals rather than diseases. The details of treatment can, therefore, be learned only by the inductive method—long-continued bedside observation of many patients under treatment—now used in teaching the subject. But back of the many details there are certain general principles which can be discussed deductively.

Pharmacology deals with only a part of these principles and then not from the standpoint of therapeutics. It deals with the physiological action of substances independently of their therapeutic effect: with the action not only of therapeutically useful substances, but also others—muscarin, curarin, and saponin, for example—whose action is chiefly harmful; and in the case of useful drugs, not only with the therapeutically important activities, but also those of no therapeutic significance. Pharmacology has developed to such an extent that it is now pursued as an independent science without

reference to the practical needs of medicine, in the same way and with the same justification that anatomy, physiology, and chemistry—once a part of practical medicine—are now pursued as independent sciences; and books are written on pharmacology, instruction is given in the subject, and research is carried on by men who are not physicians. In actual practice, drug treatment is combined with other forms of treatment—light, heat, cold, exercise, posture, diet, massage, electricity, x-rays, and high altitude—an intelligent application of which depends on a knowledge of physiology, physics, chemistry, psychology, and other factors—the personality of the physician even—as well as pharmacology. A knowledge of pathology and clinical medicine especially, though not necessary for the pharmacologist, is an absolutely necessary prerequisite for the study of therapeutics; the therapeutically important questions relating to the effect of pathological conditions in altering the effect of drug action,* and to diagnosis and prognosis which have to be taken into consideration in deciding when and how to use drugs in disease are outside the province of pharmacology.

A division of medical science dealing with the

* The reaction between a drug and a cell is far more complicated than the reaction between two chemical compounds. Stereo-isomeric differences so subtle that they almost defy detection by other chemical and physical means often alter the pharmacological action of drugs; and, conversely, differences in cells and parts of cells that can be detected in no other way can frequently be recognized by the difference in reaction to chemicals—a fact made use of in characterizing tissues by their staining reactions. It is easy, therefore, to understand how pathological changes in cells—chemical, physical, and physico-chemical changes—may alter their response to drugs.

aims and methods of therapeutics and filling in the gap between physiology, chemistry, physics, pharmacology, and the other fundamental sciences which underlie the methods of treatment, on the one hand, and the actual details of treating individual patients from day to day, on the other, should be recognized.

The most fundamental question in therapeutics is that of the **purpose** of treatment.

The treatment of acute disease aims at complete removal of disease, diseased material, or the cause of disease—the antitoxin treatment of diphtheria, and the removal of a diseased appendix are examples. Even in acute diseases like scarlet fever and measles, in which such direct treatment is not yet available, and in which the disease must be left to run its course, to be combated by the natural defences of the body itself, the result aimed at, in promoting conditions under which the body will act to best advantage, is also complete removal of all evidence of disease.

The purpose of treatment in chronic disease is often obscured by over-emphasis of the anatomical aspect of disease and under-emphasis of the physiological aspect. Though we often use the direct radical therapeutic methods of acute medicine in the treatment of chronic disease, the most important part of the treatment usually has a different objective; it has to do, not with structure, but with function. An organ may be the seat of disease, and yet, on account of the very great reserve powers of all the organs, functionally efficient (the normal heart, it has been calculated, can do six times the work ordinarily required of it;

and the factor of safety of certain double organs—since one of the pair can be removed without danger to the patient—must be at least one hundred per cent.); but with severe disease there comes a time when the affected organ cannot do the amount of work ordinarily required of it. The physician is then called in, not to make the organ anatomically perfect, but to restore equilibrium between the work required of the organ and the work which it can do; and though the diseased organ may never be made anatomically normal, it may be made functionally efficient, that is, competent to its tasks. When the heart, for example, becomes so badly affected that the amount of work it can do is less than the amount required—when compensation fails—the leaky valve or other anatomical change responsible for the condition cannot be removed or made whole. But the patient does not demand this; he wants the symptoms alleviated so that he will be more comfortable and better able to do his work; **it is not anatomical integrity that the patient demands, but functional efficiency.**

The foregoing is very important. All physiological processes are centered about adaptation of the body to the environment; this is the most fundamental principle which distinguishes living matter from dead.* In making, therefore, "equilibrium between work required and working powers"; or, expressed in broader biological terms, "adaptation of patient to environment and environment to pa-

* "In all the physiological processes which we shall study in the course of this work, adaptation will be found the constant and guiding quality," Starling, E. H., "Principles of Human Physiology," p. 5. Lea & Febiger, Philadelphia, 1915.

tient," the central principle of treatment, we are putting therapeutics on a sound biological basis; we are imitating nature.

Consider the various **methods** of treatment:

(1) *Preventive* treatment.

(2) *Direct* treatment of the disease or its cause.

(3) *Indirect* treatment of the disease or its cause; treatment directed at the functions of

(a) the heart,

(b) the lungs,

(c), (d), (e), etc., the kidneys, gastro-intestinal tract, and other organs, and

(f) the general metabolism.

In every form of disease all these groups of methods, though not equally emphasized, are borne in mind. Preventive treatment belongs largely outside the field of what is generally understood as therapeutics. Direct treatment—diphtheria antitoxin, appendectomy, quinine, salvarsan, etc.—is but yet a limited field; its aims are easily understood, and its methods relate largely to matters of detail in the technique of application; it calls for but little attention in a discussion of *general principles* of treatment. The greater part of treatment, not only in chronic disease, but also in those specific infectious diseases in which direct treatment is not yet available, is directed toward improvement in function. The basis of the trouble in chronic disease is usually a disorder of some special organ or function—the heart, the kidney, the sugar metabolism, for example—and treatment is centered around improvement in the efficiency of this organ or function. The same methods of treatment are applied in most of the acute infectious dis-

eases, but they are not centered on improvement in the efficiency of any one organ or function. Functional efficiency may be improved; equilibrium between work required and working power may be brought about—though perhaps on a lower plane than the normal—by two groups of methods:

(1) *Methods which decrease the demands* upon organs.

(2) *Methods which stimulate organs* to do better work;

and therapeutics deals largely with questions of when and how to apply such methods. **Therapeutics is, therefore, in great part a branch of applied physiology.**

For an understanding of rational therapeutics, a study of the treatment of chronic disease forms the best basis. As contrasted with the general supportive treatment of acute infectious disease, the treatment of chronic disease usually centers around improvement in the efficiency of some one organ or function; discussion and demonstration of treatment is, therefore, simpler. Changes due to the disease itself are less rapid than in acute disease, so that the effect of the treatment is more clearly discernible. The long duration of the disease makes possible a comparison of different forms of treatment in the same patient.

The treatment of chronic disease is very important. Only a small portion of the population suffers from acute disease at any one time, and the illness lasts but a short time—within a few weeks the patient is either well or dead. But a large proportion of persons who have reached middle life suffer from some weakness of function, some handicap based on

a physical defect—in its broadest sense, some form of chronic disease. To adjust such persons to their handicapped condition and thereby to maintain efficiency and comfort and to prolong life may require more or less constant medical attention.

The treatment of chronic disease is difficult. Compared with some of the clear indications for treatment in acute infectious disease—indications for diphtheria antitoxin, or for appendectomy, for example—the indications for treatment in chronic disease are lacking in precision. The severity of the disease, the degree to which functional efficiency is impaired—factors which determine the details of treatment—cannot usually be accurately measured. Their estimation is subject to great errors of judgment; and estimations of the effect of treatment on such factors—on the degree of dyspnoea, cyanosis, weakness on exertion in heart disease, for example—require not only skill and experience, but a certain amount of natural ability and aptitude. In the treatment of chronic disease, moreover, a broader view of all the circumstances of the case must be taken than in acute disease; facts concerning the patient's occupation and the state of the family and financial affairs may influence the treatment. For the few days during which they are sick, no matter what may be their family or financial responsibilities, all patients with acute disease such as pneumonia or scarlet fever usually succeed in obtaining the same excellent treatment.

Scientific methods and exact knowledge should form the basis of therapeutics. Many persons outside of scientific circles imagine that a sharp distinction can be drawn between treatment, on the

one hand, and research, on the other; that the one is intended to help the patient, the other to satisfy the idle curiosity of the doctor concerning abstract scientific problems remote from the practical needs of the individual patient. This feeling is entirely unjustified; therapeutics and research cannot be dissociated. The term scientific research implies certain intellectual methods rather than problems of any particular nature; and such methods are as applicable to the study of conditions in an individual patient as to the more abstract problems of physiology.

But very often we are obliged to abandon science and rely on empirical experience. A large part of our present therapeutic measures—inoculation for smallpox, digitalis for heart disease, caffein and other methyl purins as stimulants, cocain as an anesthetic (the list is very long)—are the result of the scientific study of facts discovered by blind empiricism. First came the empirical discovery of the facts, then the organization of the facts into science. Pharmacological research so far has been devoted largely to explaining the action of the many drugs discovered empirically. In view of such facts, it is wise not to be too skeptical of all empiricism, but to cultivate a proper measure of respect for the judgment of experienced clinicians when they state as facts that good results are obtained by methods of treatment the mechanism of which we are at present unable to understand. It should not be forgotten, too, that though the practitioner may sometimes be narrow in interpreting the rationale of some detail of therapeutics, he may, nevertheless, take a broader view of the whole sit-

uation regarding the aim of treatment than the pure scientist. The importance of scientific knowledge as a basis for therapeutics cannot be overestimated. It is not, however, by ignoring the facts acquired by empirical methods that we should try to rid medicine of empiricism, but by finding their rational basis.

From the standpoint of function, there is a natural order in which the treatment of diseases of the different systems can be discussed. The heart has but one function—that of maintaining the circulation. The general principles of treatment are practically the same whether the endocardium or the myocardium is the seat of disease; whether the lesion is one of the mitral valve or of the aortic valve. The exact anatomical nature and distribution of the lesion is of less therapeutic significance than the *severity of the disturbance of function,* as evidenced by the amount of venous congestion, edema, cyanosis, and dyspnoea. Disease of the gastro-intestinal tract is more complicated; though the same general principles—stimulation of function and rest of function—are used, and the degree of disturbance of function is of the utmost importance, there are several different functions—motor, digestive, absorptive—at which the treatment may be directed. Diseases of the kidney occupy an intermediate position. The details of treatment, at the present time, depend chiefly on the severity of the disease, on the extent to which waste products are accumulating in the body; but a case is occasionally found in which it is chiefly the tubules or chiefly the glomeruli which are imperfectly functioning—a case in which the exact distribution of the lesion is of therapeutic significance. In diseases of the

general metabolism, the disturbance of function is often not discussed as a disease of any individual organ, either because we do not know which organ is diseased, or because the cells of the body as a whole are involved. In the specific infectious diseases treatment may be directed at any or all the organs and at the general metabolism. A natural order of discussion is then: (a) heart disease, (b) kidney disease, . . . (m) gastro-intestinal disease, . . . (y) diseases of metabolism, (z) specific infectious diseases.

On account of the fact that it is usually not the anatomical lesion that we treat, but the disturbance of function, the classification of disease from the therapeutic standpoint is not always the same as from the pathological-anatomical standpoint. The anatomical classification in heart disease depends on the nature of the lesion and its distribution—factors analyzed by means of the stethoscope and graphic records. But we do not treat damaged valves or the murmurs to which they give rise. The question of first importance in determining the details of treatment is whether there is complete compensatory hypertrophy or decompensation. In examining patients for therapeutic classification emphasis should, therefore, be laid not on the murmurs, but on the efficiency of the circulation. In the case of Bright's disease the pathological anatomist distinguishes many subdivisions according to the etiological factor or the character or distribution of the lesion. From the therapeutic standpoint the question is chiefly whether the case is one with mild clinical symptoms or a severe one with edema and dropsy—a question of degree.

In the discussion which follows, the functions of the organs are briefly reviewed, and then are taken up in turn: (1) the nature of the disturbances of function brought about by disease, (2) methods of influencing these disturbances, and finally (3) the clinical forms of disease.

Question may arise as to the correctness of the physiological point of view outlined here. It cannot be denied that the facts upon which the anatomical view of disease are based are as correct as the physiological facts; but facts alone, though they are the elements from which the truth is formed, do not make the truth. The truth has many aspects, and the important thing, in determining the best aspect of a truth, lies not alone in the correctness of the facts, but in the pragmatic value—in the Kantian sense—that the point of view which results from the selection of the facts and the distribution of emphasis among the facts has as a useful productive agent.*

With this criterion of usefulness as a guide, let us contrast, from the standpoint of therapeutics, the physiological aspect of disease with the anatomical aspect.

Pathological-anatomical-bacteriological investigations have contributed much to advance the treatment of acute infectious disease in the last half century, but they have done little to advance the treatment of chronic disease. Though the death rate has decreased by one half in the last century, and the expectation of life has increased by a dozen years, the improvement is due to progress in the

* Compare Goethe's dictum, "Was fruchtbar ist, allein ist wahr."

control of acute disease. While the death rate in the registration area of the United States has decreased steadily in the last generation—19.8 in 1880, 19.6 in 1890, 17.8 in 1900, 15.0 in 1910, 13.6 in 1914—the mean death rate for persons over forty years of age, those chiefly affected by chronic disease, has actually increased—3 per cent. between 1900 and 1910, 21.2 per cent. between 1880 and 1910.

Pathological-anatomical investigations tend rather to decrease than to increase optimism. No one who is familiar from actual post-mortem examination with the terribly destructive changes found in the organs in many of the chronic diseases can believe that drugs or other treatment will restore these organs to their normal condition; even eminent practitioners, because of the difficulty of believing that treatment can influence the structural changes which the anatomical aspect of disease brings into prominence, often show a tendency to consider the so-called chronic and incurable diseases as hopeless conditions having an inherent downward tendency.

But most chronic diseases do not have a downward tendency; they result in a weakness of function; and if the functional activity of the patient is adapted to his functional capacity the status quo may not only be maintained, but often improved. It is a mistake to associate together the words "chronic" and "incurable." The dictionaries (Century, Webster) define "incurable" as "beyond the power and skill of medicine," and give "hopeless"—a term which implies that the physician is powerless—as a synonym. Though the term "incurable" may, possibly, be properly applied to those acute infectious diseases not susceptible of specific

treatment, whose course it is "beyond the power and skill of medicine" to influence directly, it should not be used with reference to such conditions as heart disease, Bright's disease, diabetes, and many other chronic diseases. We may, indeed, be unable to influence the anatomical changes found in these diseases, the anatomical changes may be incurable; but looked at from the standpoint of physiology, the disease is not "incurable." The course of the disease, the functional efficiency of the patient, is amenable to, often indeed, largely determined by treatment. A patient whose leg had been amputated would not be sent away with the statement that, since it is impossible for him to grow a new leg, nothing can be done for him. By the use of an artificial leg, and by refraining from certain activities, such a patient can become nearly as efficient as a normal man. The same attitude should be taken toward patients with incurable lesions of internal organs; these patients, too, can often be made functionally efficient.

All this bears directly on the question of the correctness of the physiological point of view. This optimistic point of view is surely a more useful guide; has greater pragmatic value in therapeutics than the pessimistic anatomical point of view. And since usefulness, pragmatic value, determines the correctness of a scientific truth, the anatomical point of view is a wrong one from the standpoint of therapeutics and the physiological point of view is the correct one.

# DISEASES OF THE HEART.

## General Principles of Treatment.

When, as a result either of incompetent valves, a weakened musculature, or, even improper nervous control, the efficiency of the heart is so greatly decreased that it becomes incompetent to carry on its work; when there is a loss of equilibrium as a consequence of a preponderance of the work to be done over that which the heart is doing, and venous congestion, edema and other symptoms arise, it is the aim of treatment to restore equilibrium. To do this we employ:

(*a*) *Methods to decrease the work which the heart is called upon to do;*

and, at the same time,

(*b*) *Methods to stimulate the heart to utilize its power more effectively.*

This, indeed, is nature's method of compensating. In cases of heart disease the heart usually increases its activity by undergoing hypertrophy; and the patient, if he heeds nature's warnings, decreases his activities.

## Methods of Decreasing the Work Required of the Heart.

The demands upon the heart may be decreased by:

(1) Decreasing metabolic activity.
(2) Decreasing nervous and mental activity.
(3) Relieving the body of fluid.
(4) Decreasing abnormally high blood pressure.

**Decreasing Metabolic Activity.** The metabolism may be decreased by **diminishing muscular activity and by dietetic measures.**

All kinds of **muscular effort** make increased demands on the circulatory apparatus; the blood pressure rises and the work of the heart is increased. The response to increased muscular activity on the part of the heart is very prompt and, possibly, due, in part at any rate, to stimulation of the center in the medulla; this stimulation results from the higher hydrogen ion concentration of the blood, the result of increased formation of carbonic acid and other acid end products of metabolism. Absolute rest in bed makes the least demand on the heart, and is indicated in all cases of heart disease with failure of compensation. Rest in the horizontal position in bed gives the nearest approach to absolute muscular rest, but in many cases of heart disease a semi-recumbent position is best; partly because respiration is thereby made easier; partly because, as a result of pressure on the phrenic nerve in some cases of heart hypertrophy, rest in the horizontal position may be followed by an increase in the heart rate. Rest after meals, especially, is advisable; an increase in the blood supply of the splanchnic area and of the musculature at the same time

obviously puts a strain upon the heart. Even when there is edema and dilatation, several days' rest in bed is often sufficient to restore compensation. In less severe grades of heart disease one of the tasks of the physician, and one for which definite rules cannot be laid down, is that of properly regulating the muscular activity of the patient.

The metabolism may be decreased by **dietetic measures.** Large quantities of food increase the metabolism and, therefore, the work required of the heart, and lead, furthermore, to the deposition of adipose tissue, which still further increases the work of the heart. If the patient has too great an accumulation of adipose tissue, the excess should be removed by suitable measures; if not, he should be given just enough food to maintain weight. If too little food is given the patient loses strength. With patients who are anemic and much under weight it may even be necessary to increase the amount of food taken. The rule is to give just enough food to maintain the strength and keep the patient at normal weight.

**Decreasing Nervous and Mental Activity.** It is now well recognized that as a result of action through the sympathetic nervous system and glands of internal secretion, increased nervous and mental activity leads to constriction of the smaller arteries and a rise of blood pressure, and increases the work of the heart. Patients with heart disease should, therefore, lead a quiet life, as free as possible from all worry, care, and excitement. The penalty for undue excitement and worry is often increase in the rate of the heart, increase in the physical signs of impairment of circulation, sudden onsets of dis-

tressing subjective symptoms; sometimes, indeed, sudden death. In order to quiet the patient it may often be necessary to resort to drugs. Bromides and other hypnotic drugs are sometimes used. Under certain circumstances, morphine is excellent. When the dyspnea, palpitation, cough, pain, anxiety, and distress are severe, the strain on the heart from the over-active metabolism, and the failing nutrition resulting from loss of sleep may do much harm; in such cases the quiet and rest following the use of morphine often give the heart the needed opportunity to restore compensation. On the ground that drugs containing chlorine have a dangerous depressing action on the heart, some pharmacologists advise against the use of chloral in cases of heart disease, but clinical experience has not shown that it is especially dangerous if used carefully; it is better, however, not to use it if fatty degeneration of the heart muscle is suspected.

**Relieving the Body of Fluid.** The amount of work which the heart has to do depends in part on the amount of fluid which it must pump through the circulatory system. In cases of impairment of cardiac function accompanied by accumulation of fluid in the venous system and in the tissue spaces, one set of measures is aimed at preventing this accumulation and, when it is present, removing it. The removal of fluid may be promoted by stimulating excretion through: (*a*) the *bowels,* (*b*) the *kidneys,* (*c*) the *skin*—organs through which fluid is normally excreted—and, when quick removal of fluid is more imperative, by (*d*) *tapping* serous cavities, (*e*) *draining* the subcutaneous tissue, and (*f*) *venesection.* The signals for active stimulation of the

bowels, kidneys, and skin, are venous congestion, and the collection of fluid in the subcutaneous tissue, and serous cavities.

When retention of fluid is marked, it may sometimes be advisable to decrease the **fluid intake**, but there is considerable difference of opinion regarding the advisability of this measure and the extent to which it should be used. If the **fluid intake is restricted**, the output should be measured to make sure that the urine does not become so concentrated as to irritate the kidneys. The rule is that an excessive quantity of fluid should not be ingested.

To stimulate excretion through the **bowels**, the hydragogue cathartics—the sulphates, phosphates, citrates, tartrates, and carbonates of sodium, potassium, and magnesium—are especially useful; they do not cause much gastro-intestinal irritation. The belief in their power to deplete the blood and promote absorption of lymph from the tissue spaces, as a result of attracting water into the intestine, is probably somewhat exaggerated; the amount of water lost in this way is not great as a rule, but they do relieve the work of the heart entailed by straining at stool. Magnesium sulphate—Epsom salt—is much used; from a drachm to an ounce or more given on an empty stomach from half on hour to an hour before breakfast will usually be followed by several liquid evacuations. Compound jalap powder in half drachm doses is often used. Other cathartics—in advanced cases even drastics—may be required.

The **kidneys** may be stimulated to increased activity by diuretics. The milder diuretics may be used at first—the sodium and potassium salts of

citric, acetic, tartaric, and other aliphatic acids; these oxidize to bicarbonates, and it is the bicarbonates which act as diuretics. The diuretic action of these salts is not entirely understood; it may be due to the fact that the bicarbonates formed, not being easily diffusible, do not readily pass from the blood into the tissues, water instead being attracted by them from the tissues into the blood, and the resulting hydremia leading to diuresis*; or the hydremia may be due in part to their effect in decreasing the hydration water (discussed under nephritis) of the blood and tissues.

More active diuretics, members of the caffein group—caffein, theobromin, theophyllin—may be used. These act directly on the protoplasm of the kidney cells and stimulate them to increased activity. They have also a stimulating action on the central nervous system as well, an action which is antagonistic to that on the kidneys. When reflex irritability is increased, this central action—especially marked in the case of caffein, less marked with the others—may completely overcome the diuretic action. The central action of caffein can usually be suppressed by a small amount of a hypnotic drug—a small amount of an alcoholic drink, for example. The diuretics of the caffein group are insoluble and, therefore, commonly administered in the form of soluble double salts; diuretin, for example, is the double salt of sodium theobromin and sodium salicylate. The body quickly acquires a tolerance for these diuretics; after they have been given for a short time they may fail to act, and may

* This is the explanation commonly given; but it is diffisult to see how it can apply, since oxidation takes place, not in the blood stream, but in the cells of the body.

even cause suppression of urine. One of the best modes of administration is to give three doses of the drug (2 grains caffein, 3 grains of theophyllin, or 10 grains of diuretin) and then not repeat for a day or two.

In very severe conditions, when other diuretics have proved ineffective, calomel, in three-grain doses every three to six hours, sometimes gives striking results. The teeth should always be watched after administration of calomel; the drug has a tendency to make them sore and loose. When suppression of urine is due to poor nutrition of the kidney resulting from venous congestion, drugs of the digitalis group, which stimulate the heart to work more efficiently, act as diuretics.

The elimination of waste products through the skin may be promoted by baths; but great care should be used in prescribing baths in heart disease. Too hot or too cold baths, especially if they increase the heart rate, should be avoided. Hot baths are liable to cause irritation of the nervous control of the heart; they put an extra strain especially on the vasomotor center; then, too, especially if the patient shows asthmatic tendencies, they increase respiratory difficulties. Cold baths increase the metabolism and may, therefore, be dangerous. Moderately warm baths, which decrease heat production and thus indirectly diminish the work required of the heart, may be good. When we desire to influence the nervous control of the heart, and in conditions in which it is desirable to stimulate the heart directly, moderately cold, stimulating baths may be useful. As a rule, however, the skin should be kept active in heart disease only by mild measures,

daily sponging with tepid water, for example; and the lowered tone and the dilatation of the vessels of the skin resulting from the tepid baths should not be overcome, as in normal persons, by cold spraying, but by wrapping in warm blankets and by massage. In spite of numerous studies of the effect of bathing in pure water, salt water, and carbonated water, on the blood pressure, pulse rate, and other factors involved in heart disease, exact indications for baths cannot be given; we must always be guided by the whole clinical effect on the individual patient.

In addition to promoting elimination of fluid through the bowels, kidneys, and skin—channels through which fluid is normally excreted—more **direct removal of fluid** may be necessary. Serous cavities—pleural, peritoneal, pericardial—may be tapped when fluid accumulates in them. Blood itself may be removed by venesection. Incisions may be made into the subcutaneous tissue of the legs, or a silver cannula (Southey's tube) inserted, and the edematous fluid allowed to escape directly. The accumulation of such fluid is sometimes part of a vicious circle leading to complete suppression of urine; with its removal secretion of urine often promptly begins again. The signal for tapping, scarifying, or tubes, is the presence of large quantities of fluid in the serous cavities or subcutaneous tissue which does not disappear under less direct forms of treatment.

When congestion of the venous system becomes very great, leading to acute dilatation of the right side of the heart with suppression of urine, marked cyanosis, and respiratory distress, **blood itself may be removed**; the cephalic vein can be severed at the

bend of the elbow under aseptic precautions, after placing a tourniquet around the upper arm, and several hundred cubic centimeters of blood allowed to escape. Within a few minutes, usually indeed, before the blood-letting is finished, the weak, rapid, irregular pulse becomes slower, firmer, and more regular; and the subjective symptoms show decided improvement. The operation will sometimes save a patient's life. The indications for venesection in heart disease are acute dilatation of the right side of the heart, pulmonary edema, venous central hyperemia, and threatened heart paralysis.

**Reducing Abnormally High Blood Pressure.** The work required of the heart may be diminished by decreasing unduly high blood pressure, often present in so-called cardiorenal disease. The nitrites—amyl nitrite, nitroglycerin, and sodium nitrite—cause paralysis and dilatation of the smaller arteries and lead to a fall of blood pressure. Amyl nitrite is not used clinically for this purpose, its effect being too evanescent; sodium nitrite and nitroglycerin, whose action lasts longer, are used instead. Nitroglycerin is not to be swallowed, but allowed to dissolve on the tongue; it is absorbed more rapidly and certainly in the mouth than in the stomach. The indication for the use of nitrites is very greatly increased blood pressure. Special hydrotherapeutic measures, particularly the form of baths given at Nauheim—moderately warm baths containing carbon dioxide—are useful.

## Methods of Stimulating the Heart.

The object of the methods outlined in the foregoing paragraphs is to improve the circulation by

relieving the heart of as much work as possible. In the treatment of severe heart disease, these methods are combined with other methods whose object it is to improve the circulation by stimulating the heart itself to work better. The chief method employed for this purpose is the use of drugs of the digitalis group—digitalis, strophanthus, squills, apocynum.

Digitalis improves the efficiency of the heart action. The normally beating heart does not use all its reserve force. Normal systole is not complete; the dog's heart has been shown to be as much as one-third full after systole. Normal diastole is not complete; the dilatation is not so great as after stimulation of the vagus, or as when the heart is relaxed after death. In a pathologically rapid and irregular heart, moreover, the shortened time interval for each beat makes a still less complete systole and diastole necessary. Under the influence of therapeutic doses of digitalis, the heart dilates more completely in diastole and empties itself more completely in systole so that the pulse volume is increased; an increase in the systolic output of each ventricle as much as threefold has been demonstrated. This effect on the heart muscle is supplemented in pathologically rapid hearts by the effect on the conducting mechanism. Digitalis renders this mechanism less sensitive and makes the heart rate, therefore, slower and more regular; the greater time allowed for each beat permits more complete systole and diastole. Since, then, the result of digitalis action is to make systole and diastole more complete, the effect is, therefore, greatest in hearts in which systole and diastole are least complete. In other words, the improvement in efficiency is greater

in diseased hearts than in normal hearts—a difference noted also in animal experimentation, the greatest effect being seen in hearts which have been somewhat damaged by manipulation. With the more complete filling and emptying of the heart under the influence of digitalis, there is a more complete filling of the arteries; the improvement in circulation hastens the flow of interstitial fluids and favors its resorption. Furthermore, as a result of the improvement in the nutrition of the tissues, the nutrition of the heart itself improves, and this organ shows a greater tendency to compensatory hypertrophy. Digitalis acts also on the arteries in some portions of the splanchnic area, especially in the portal circulation—a region in which stasis and overdistention is marked in decompensated heart disease—constricting them and raising their tension so that a more steady flow of blood is maintained in the capillaries. The renal vessels, however, do not share in this constriction. There is, indeed, evidence that they dilate; so that, while the stasis in the large abdominal organs is overcome, the blood supply of the kidney is increased. On account of the complexity of the action of digitalis on the heart muscle itself, on its nervous and conducting mechanism, and on peripheral vessels it is, at present, difficult to ascribe to each action its relative therapeutic importance. Some pharmacologists lay great stress on the direct action upon the heart muscle; others emphasize the effect on the conducting mechanism; and many believe that the doses required to affect the abdominal vessels are so large that the action on these vessels is of little therapeutic significance.

Digitalis may be used in heart disease of all kinds when compensation has become broken, with a resulting incomplete filling of the arteries, engorgement of the venous system, and accumulation of fluid in the interstitial tissue. The general rule is not to give the drug when there is perfectly balanced compensatory hypertrophy. The infusion or the tincture, or one of the active principles, digalen or digipuratum, may be used—the important thing being to use an active preparation. If no effect is obtained from the particular preparation used, other preparations should be tried before giving up digitalis therapy. After administration of digitalis, the urine should be measured; within twenty-four to forty-eight hours, as a rule, the flow of urine is increased, the dyspnea is relieved, the edema disappears, the pulse becomes slower, firmer, and more regular. Administration of the drug may be discontinued when the pulse rate falls to sixty or eighty. If no effect is observed in four or five days, the dose may be increased until either the therapeutic effect is obtained or until untoward symptoms appear.

In some cases the effect of a short course of digitalis therapy on compensation may be permanent; or, at any rate, compensation may subsequently be maintained for a long time without any further use of digitalis. In other cases compensation may begin to fail as soon as digitalis is discontinued, and it may be necessary to continue the administration of small doses for a long period. In still other cases it may be necessary to continue to give large doses of digitalis to keep the pulse rate down and maintain compensation; in such cases as the latter, ad-

ministration of the drug should be interrupted from time to time or whenever symptoms of gastro-intestinal irritation—nausea, vomiting, diarrhea—appear. Which of these grades of severity we are dealing with in any particular case can be determined only by experiment. It seems reasonable to suppose that a heart which is constantly over-stimulated with drugs will tend to exhaustion; we should, therefore, use digitalis and other heart stimulants no more than is necessary.

Some patients do not react well to digitalis; the pulse may drop very low—to 45 or less—or the rate may not fall at all, but increase instead, or the pulse may become weak, or the patient may become more cyanotic, or there may be a sudden decrease in the excretion of urine. All these are important danger signals, and indicate that the drug should be discontinued. If a patient does not respond to digitalis therapy, or is intolerant to it and responds badly, or if portal stasis or some other condition of the gastro-intestinal tract makes the use of digitalis inadvisable, other members of the group—strophanthus, squills or apocynum—may be used. When a quick result is desired, 1/250th of a grain doses of strophanthin in 40 to 60 minims of normal saline solution may be given intravenously. On account of the irregularity of absorption, intravenous administration of strophanthus is better in any case than administration per mouth.

Other drugs which stimulate the heart are caffein, strychnine, camphor, and ammonia compounds. These drugs act directly on the heart muscle and on the vasomotor areas in the medulla, the latter action leading to vasoconstriction. They are, there-

fore, used less in real heart disease than in acute infectious diseases—pneumonia, bronchopneumonia—and after surgical operations where the circulatory failure is predominantly vasomotor. Epinephrin has been successfully used to combat vascular depression; it directly stimulates both the heart and the vessels. Its action is quick in appearing but rapidly passes off; it is, therefore, used to combat vascular depression when quick action is imperative to tide over a brief period of imminent peril, until other slower-acting drugs or methods of treatment have become effective, or when the circulation needs support for only a short time.

Although, as a rule, metabolic and muscular rest is prescribed for persons with heart disease, yet, under certain circumstances, for the purpose of improving the strength of the heart, graduated exercises should be prescribed. A system of exercises devised by Schott will be found in the text-books, but almost any kind of muscular exercises will do, provided they are mild in character and carefully adapted to the individual patient. It is difficult to say in advance which cases of heart disease will be helped by exercise. Rest, not exercise, is indicated in cases with edema, dyspnea, and other signs of failure of compensation; carefully graduated exercises are more useful in certain cases of arrhythmia of nervous origin. The amount of exercise permitted should be regulated by its effect on the clinical condition; it should be decreased at once on any aggravation in the clinical condition. It is well, at least, to provide the patient with some kind of occupation, if possible, to take up his time.

## Other Details of Treatment.

In addition to the more direct methods of influencing the circulation, any factors which contribute to the heart disease should be treated, the general hygienic environment should be made as good as possible, and troublesome subjective symptoms combated.

**Contributing Causes.** Any pathological condition in the body that can be considered a contributory cause, especially any form of bacterial infection, should be treated. Patients with rheumatism may be given salicylates; those with syphilis, potassium iodide, mercury, or salvarsan. Attacks of acute cardiac weakness and irregularity can sometimes be stopped by removal of a focus of infection in the tonsils, teeth, or elsewhere. Faulty nutrition resulting from anemia may contribute to the heart weakness. The nutrition of the heart suffers equally with that of other organs in this condition, and a heart that is badly nourished fails to do its work; the anemia should be treated.

**General Hygiene.** Tea, coffee, alcohol, and tobacco may all have an injurious effect on the heart and should, therefore, be restricted or forbidden. Excessive quantities of beer seem to be especially harmful. Tobacco may aggravate irregularities, accelerate the rate, and make anginal attacks more frequent. Catarrhal conditions in the respiratory tract can increase the work of the right side of the heart and should, therefore, if present, be relieved. Suitable measures should be adopted to protect the patient from catching cold. A warm, dry climate, not subject to rapid changes of temperature, is the

one best suited to patients with heart disease. A high altitude and rapid changes of temperature stimulate the nervous system and the metabolism, and increase the work required of the heart. A warm climate, on the other hand, relieves the metabolism of a certain amount of stimulation, and quiets the nervous system; a dry climate keeps the skin active. Gastro-intestinal disturbances leading to flatulence and dilatation of the stomach have an unfavorable effect on the heart, and should be treated; cabbage, peas, beans, potatoes, and carbonated drinks are especially liable to cause flatulence and to be followed by increasing shortness of breath and palpitation. Constipation should always be relieved.

**Subjective Symptoms.** The subjective symptoms are the result of the disturbance of circulatory function, and are relieved when function is improved; but certain subjective symptoms may sometimes be helped by more direct treatment.

Patients who are **dyspneic** or **asthmatic** and unable to breathe comfortably when lying down, should be provided with a comfortable bed rest. When the dyspnea or asthma is severe and interferes with proper rest, the use of morphine or its derivatives may be considered.

For **sleeplessness** alcoholic drinks and other hypnotics may be used. Chloral is also used, and intravenous injections of strophanthin are said to be good. Morphine is especially effective in relieving pain, and in quieting the respiratory center; it is, therefore, a good rule to use morphine in cases of sleeplessness *only* when the sleeplessness is due to pain, coughing, and dyspnea.

**Palpitation and cardiac distress** are sometimes relieved by an ice bag over the heart, by aconite, by potassium iodide or nitroglycerin; when due to nervousness bromides are good. These symptoms are often due to flatulent distention of the stomach.

All sorts of measures are found at times to relieve the great distress accompanying attacks of **paroxysmal tachycardia.** The patients themselves often discover that certain postures or dietetic measures afford relief. Good hygiene, opiates, digitalis, an ice bag, may all give prompt relief, and may sometimes all be ineffective.

**Pains around the heart** may sometimes be relieved by application of an ice bag over the heart, by opiates, or by strapping the side with strips of adhesive plaster. Potassium iodide is useful for the pains in aortic disease. For the pain of angina pectoris nitrites may be used. If the attacks are frequent and last but a short time, pearls of amyl nitrite may be broken in the handkerchief and the fumes inhaled; amyl nitrite should be taken lying down, otherwise the patient may become dizzy and fall. The effect of amyl nitrite is quick to appear and quick to pass off, so that if the attacks of angina are frequent or lasting, nitroglycerin or sodium nitrite are better. The attacks may be so severe that morphia or inhalations of ether may be necessary. Excitement and over-exertion often bring on attacks, and should, therefore, be forbidden. If this is impossible, nitroglycerin may be given before the exertion to ward off the attack. Digitalis often proves useful in cases of angina. Small doses of potassium iodide are valuable for diminishing the frequency of paroxysms.

The **cough and hemoptysis** resulting from congestion of the pulmonary vessels are rarely serious enough to require direct treatment.

The **gastric symptoms**—nausea, vomiting, loss of appetite—associated with engorgement of the vessels of the liver and stomach are difficult to affect directly. Bits of ice, effervescing drinks, milk and limewater may sometimes help.

Many other measures are found useful in treating the subjective symptoms, but these are more appropriately discussed in the special text-books.

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## Forms of Heart Disease.

It is clear that the forms of treatment outlined for heart disease are not directed at any valve or other particular anatomical structure of the heart, but at the function of circulation as a whole, the aim being to improve the functional efficiency of the circulation; the same general principles are, therefore, used in the treatment of all forms of impairment of circulation, no matter what the anatomical defect which is responsible. In the classification of heart diseases from the therapeutic standpoint, it is not the anatomical nature and distribution of the lesion that is the determining factor in directing the treatment—although this is of importance in modifying the details of treatment—but the degree to which function is disturbed. From the therapeutic standpoint, the two chief classes of heart disease are (a) those with complete compensatory hypertrophy, and (b) those with failure of compensation. An example of the significance

of this classification is seen in the signal for the use of digitalis. The fact that different physicians might not agree on exactly what degree of severity might be taken as the sign of failure of compensation in any particular case, and that in order to maintain compensation in certain cases it is sometimes found necessary, as has already been pointed out, to continue digitalis therapy even when there are no marked signs of failure of compensation, does not invalidate the general rule that the signal for the use of digitalis is failure of compensation.

Cases of heart disease showing no signs of failure of compensation may be further conveniently divided into two classes, acute and chronic. We may possibly speak even of a condition of potential heart disease—a condition treated by preventive measures. It has been observed, namely, that acute heart disease is less frequent as a sequel of such diseases as chorea, rheumatism, and eruptive fevers in those patients who have been kept at rest in bed throughout the whole course of the disease; and it is said that a threatened attack on the heart in such conditions may sometimes be prevented by active purgation.

**Acute Heart Disease without Failure of Compensation.** In all cases of acute heart disease, even when there is no sign of failure of compensation, the patient should be kept quietly at rest in bed, free from excitement, care and worry until all evidence of acute disease is past; the bowels and skin should be kept active, and the diet low; sometimes no other treatment may be necessary.

**Chronic Heart Disease without Failure of Compensation.** When valvular disease or other evidence

of abnormality in the heart is discovered in the course of the physical examination of a patient showing no evidence of failure of compensation, no drug treatment or other active therapeutic measures need be instituted. Either the patient or some member of the family may be told that the heart is weak and cannot stand excessive strains. It may not be necessary to keep the patient in bed; if it does not cause distress he can be allowed to exercise in moderation. The diet should not be abundant enough, on the one hand, to cause increase in weight, or restricted enough, on the other, to cause a loss of strength and lead to under-nutrition. On account of their action on the heart, tobacco, alcohol, tea, and coffee should be used, if at all, only with moderation. The skin should be kept active with daily tepid baths, and the patient should have a daily soft evacuation of the bowels.

**Heart Disease with Failure of Compensation.** When compensation has become broken, all the various methods outlined in the foregoing paragraphs are at our disposal. Only the mildest measures are used at first; rest in bed for a few days may alone suffice to restore compensation. Cathartics and dietetic measures can next be added to the treatment, other drugs only as a last resort. The first evidence of heart disease may be the sudden death of the patient. More commonly, however, there is gradually increasing shortness of breath, and dyspnea, especially at night and on exertion; and anemia, signs of impaired nutrition, and a decreased adaptability of the heart to demands upon it, are often present. With more serious weakness, the heart may be dilated, and edema, dropsy, cyanosis, marked dysp-

nea, venous visceral congestion, and forms of arrhythmia may be present. These are the signals for the use of digitalis. Auricular fibrillation, too, is an indication of severe muscular damage, and usually indicates impending cardiac failure. Digitalis is indicated in this condition if the rate exceeds 100 when the patient is at rest.

**Other Forms of Heart Disease.** With certain modifications, the same general methods of treatment are applicable in cases of cardiac insufficiency due to myocarditis, pericarditis, arteriosclerosis, and nephritis, as well as valvular disease. Digitalis is useful in all forms of heart disease with failure of compensation. The important thing to consider is the efficiency of the circulation. The details of the treatment, however, depend somewhat on the nature of the lesion. The best results from digitalis are obtained when the heart muscle is in good condition; when the heart muscle is badly damaged the results may be nil. The effectiveness of digitalis, for example, is not the same in different forms of heart disease. The clue to the difference lies in the fact that digitalis does not increase the absolute power of the heart, but merely stimulates the heart to exert its power more effectively; its effect is greatest, therefore, when the heart muscle itself is in good condition, and may be nil when the heart muscle is badly damaged. In cases of mitral insufficiency accompanied by that form of tachycardia known as auricular fibrillation, for example, a condition resulting from insufficiency of the valves and appearing first while the heart muscle itself is still in relatively good condition, the effect of digitalis is most marked and the drug acts often almost

as a specific. In aortic disease, on the other hand, the powerful left ventricle compensates for the insufficient valve for a long time, and signs of decompensation do not appear until, as a result of fibrous myocarditis, or coronary sclerosis, the heart muscle itself gives out. Under such circumstances digitalis is less effective and larger doses are required.

In cases of **myocarditis,** venous congestion and edema may be less prominent symptoms, sometimes even absent; instead, there may be marked arrhythmia with feeble, irregular, slow pulse, and attacks of angina. In such cases, digitalis may not be very effective; other stimulants—aromatic spirits of ammonia, small doses of strychnia—are given.

In the **neuroses** of the heart—various forms of arrhythmia of nervous origin—digitalis is not indicated; rest is usually indicated. The patient should lead a quiet life, free from all excesses and excitement. He should take plenty of sleep, use moderation in eating and drinking, and keep his bowels active. Attempts should be made to remove the cause of the nervous condition; intestinal parasites or other gastro-intestinal disturbances, and the excessive use of tobacco, tea, and coffee are sometimes responsible. Massage, tepid baths, and graduated exercises to strengthen the heart are helpful. Iron and strychnine are useful. Bromides, and occasionally other hypnotics, may be required to allay the nervousness.

In **congenital heart disease,** digitalis, though occasionally of value, is not much used. Especial attention is directed in these cases to nourishing the child and keeping it warm; otherwise the principles

of treatment are similar to those of other forms of heart disease.

In cases of **pericarditis** especial attention is given to all the different methods of resting the heart; absolute rest in bed is very important. In robust patients, venesection may be helpful. An ice bag over the heart, or counter-irritation from a blister or leeches may retard the progress of a beginning effusion as well as relieve the distress. When effusion is present, absorption is hastenend by counter-irritation and by promoting the excretion of water, but by mild measures only, through the bowels, kidneys, and skin. When the effusion is great enough to impair seriously the heart action, the pericardium may be tapped. When the effusion is purulent, the pericardium should be drained by the surgeon.

In the various infectious diseases and after surgical operations, the efficiency of the circulation may become impaired as a result of **vascular depression** and accumulation of large quantities of blood in the splanchnic area; in such cases, the pulse becomes weak, rapid, and irregular, and the skin shows pallor, and, sometimes, cyanosis. Digitalis and the therapeutics for heart disease are not indicated; substances like camphor, ammonia, strychnine, and caffein, which act not only on the heart but also on the vasomotor center, are used instead. Alcohol, and subcutaneous injections of ether are also given; how these latter act is not entirely clear,—probably reflexly from the local effect. Saline infusions are administered to help fill the vessels.

The foregoing discussion of the forms of heart disease is intended to bring out the physiological point of view in classification. The different forms

are not, therefore, taken up under the usual pathological-anatomical-clinical names. But this need cause no difficulty. Take, for example, subacute endocarditis, a condition not specifically mentioned here by name, in which periods of almost perfect health are suddenly interrupted by attacks of failure of compensation. Since this condition is either heart disease without failure of compensation or heart disease with failure of compensation, nothing need be added to the discussion. (In so far, however, as the condition may also be a specific infectious disease consult the chapter on specific infectious diseases.)

# DISEASES OF THE KIDNEY.

In diseases of the kidney, as in diseases of the heart, the object of therapeutics is not to restore anatomical integrity but to improve functional efficiency. We have at our disposal no means of stimulating the regeneration of new tubules and glomeruli to take the place of those which have been destroyed, or of restrainng the connective tissue proliferation. But when the kidney is diseased to such an extent that failure of equilibrium between the work required of it and the work it can do leads to the retention of waste products within the body we can often restore equilibrium on a new plane by decreasing the work required of the kidney and, at the same time, increasing the power of the kidney to do work.

Further evidence of the importance of physiology rather than anatomy in treatment is shown by the fact that though the kidney and the heart have an entirely different anatomical structure and do work of an entirely different character, yet the general methods of treating kidney disease are nearly the same as those for treating heart disease. In a general way, those methods which rest and stimulate the heart function have the same effect on kidney function. Furthermore, hypertrophy of the heart frequently results from severe kidney disease and a lowered efficiency of the kidney from severe heart disease; in the later stages we are called upon, therefore, to treat so-called cardio-renal disease.

The kidney is made up of groups of long tubes twisted and folded on themselves; these unite and empty into the pelvis of the kidney; the swollen blind end of each tube, the glomerulus, is invaginated by a tuft of capillaries. The old hypothesis that the water and solids of the urine are all secreted into the glomerulus by simple physical processes of diffusion, osmosis, and imbibition, and that the urine is later concentrated in the tubules by diffusion of water back to the more concentrated lymph, has largely been given up in favor of the hypothesis that the secretion of urine is not a simple process entirely explained by the physical and chemical laws of diffusion and osmosis, as we now understand them, but a process due to a specific, and, as yet, unexplained activity of the cells of the glomeruli and tubules analogous to the process of secretion by other glands. According to this hypothesis, the cells of different parts of the tubes have different functions, that of the cells of the glomeruli, for example, being chiefly the secretion of water and common salt; that of the cells of the convoluted tubules chiefly the secretion of urea, uric acid, and other end-products of nitrogenous metabolism. For this reason, it is theoretically possible to have disease of the glomeruli or disease of the tubules with a resulting difference in the functional disturbance and, indeed, such conditions are sometimes recognizable and make the treatment of kidney disease slightly more complicated than that of heart disease; but the results of recent pathological and chemical studies are making it more and more evident, that, in the clinical forms of kidney disease, all elements of the kidney, and the secretions as a whole, are

usually affected and that, therefore, as in heart disease, difference in severity of the disease is the chief factor of importance for a therapeutic classification.

For an understanding of certain hypotheses and theories relating to the secretion of urine, the treatment of edema, and the action of certain diuretics, it is necessary to recognize two kinds of water in the blood and tissues: part of the water—the so-called "hydration-water," together with its dissolved crystalloids, is united in the form of a loose chemical combination with the colloids, giving a compound similar to jelly; the rest of the water with its dissolved crystalloids is "free." Only the free water and its crystalloids are immediately available for secretion into the urine. The proportion of "free" water to "hydration" water may vary; the factors on which it depends are not entirely understood but the composition of the colloid and the amount and character of the crystalloids in the solution influence it.

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## General Principles of Treatment.

The purpose of treatment in kidney disease is to prevent the accumulation of the end-products of metabolism which may be retained as a result of imperfect functioning of the kidney. To fulfill this purpose we

(a) Diminish the work which the kidney is called upon to do by:

  (1) Decreasing the formation of those waste products which are excreted through the kidney.

(2) Decreasing nervous and mental activity.
(3) Stimulating the activity of other organs through which waste products may be removed, and,
(4) Directly removing fluid—t a p p i n g, venesection.

In addition, we

(b) Stimulate the secreting power of the kidney itself

(1) By the action of diuretics.
(2) By improving the nutrition of the kidney through the use of heart stimulants.

In addition we improve the general hygienic environment of the patient and treat the subjective symptoms. By decreasing the work required of the kidney, and, at the same time, stimulating its excreting powers, equilibrium between the work required of the kidney and the work which it can do may again be reached and the functional efficiency of the organ and of the patient improved.

## Diminishing the Work Required of the Kidney.

**Decreasing the formation of waste products.** We can decrease metabolic activity by decreasing muscular work and by dietetic measures.

Whether or not, in cases of nephritis, all **muscular activity** should be prohibited depends on the severity of the disease. In acute nephritis following infectious diseases, and in the severer stages of chronic nephritis, absolute rest in bed is essential. In moderate grades of chronic nephritis a certain amount of exercise may be necessary to avoid gastro-

intestinal disturbances, headache, and other symptoms. No definite rules for the amount of exercise in individual cases can be laid down; clinical experience with many other cases, supplemented by experiment in the case under treatment, is the only guide.

Great moderation should be observed in **eating and drinking.** In acute Bright's disease, and in the severer grades of chronic Bright's disease, clinical experience has demonstrated the value of a strict milk diet. Children, especially, can stand such a diet for long periods; in older persons it may cause loss of appetite, constipation, and headache; in such cases gruels made of barley, oatmeal, or arrowroot can be added. If an exclusive milk diet contains too much fluid for the patient, part of the milk may be replaced by cream or by carbohydrate gruels. Clinical experience indicates that protein food—probably on account of the large quantity of nitrogenous end-products which have to be excreted through the kidneys—especially meat and fish, should be restricted; it can be replaced, in part, by carbohydrates and fats—the end-products of whose metabolism (carbon dioxide, and water) are excreted largely by other organs. Meat soups should be restricted on account of their content in extractives—purin compounds and other nitrogenous bodies which are excreted through the kidneys. Carbohydrates are well borne. Fats, in large quantities, may cause gastro-intestinal disturbances. Green vegetables—except those like asparagus, parsley and celery containing oils which may cause renal irritation when taken for long periods—may be given.

On the ground that excretion of water adds to

the work of the kidney, physicians sometimes restrict the fluid intake. But experience shows that the more concentrated urine resulting from this restriction sometimes irritates the kidneys and leads to an increase in the albumin, casts, and cells, and that, furthermore, it increases the gastro-intestinal disturbances, and the severity of the subjective symptoms; patients are, therefore, usually advised to drink carbonated waters, lemonade, and other mild diuretics freely.

In many cases with dropsy and edema, the retention of fluid is due not to an inability of the kidney to excrete water but rather to a retention of salt (NaCl) in the tissues. In these cases, the water retention is secondary to the salt retention and promptly disappears on excluding salt from the diet and administering only foods poor in salt.

**Decreasing nervous and mental activity.** The patient should be kept as free as possible from excitement, care, and worry; excitement, exertion, mental disturbances of all kinds cause the blood pressure to rise—a bad sign in nephritis—and the other symptoms to become worse; with a quiet life, free from care, excitement, and other mental disturbances, the blood pressure falls and the other symptoms improve.

**Promoting elimination of waste products through other channels.** End-products of metabolism may be excreted in part through the bowels and the skin, and, in all forms of kidney disease, the kidneys may be relieved of part of their work by maintaining active excretion through these other channels. In mild forms of chronic nephritis, it may be necessary to use only an occasional mild laxative; in severer

cases, with edema, and dropsy, larger doses of the hydragogue **cathartics** may be used. These saline cathartics are especially efficacious when there is retention of water in the tissues; they deplete the blood and thereby hasten the flow of interstitial fluid into the blood stream. Magnesium sulphate—Epsom salt—given on an empty stomach half an hour to an hour and a half before breakfast in doses of a drachm to an ounce or more is much used, also aloes and compound jalap powder. In uremic or unconscious patients some of the drastic vegetable purgatives may be required.

Elimination of water and solid waste products **through the skin** is stimulated by warm baths and hot packs. Suppression of urine and symptoms of impending uremia are often promptly relieved by a thorough sweating. Not only water but also inorganic salts and organic substances in appreciable quantities are excreted through the skin. Even when at entire rest and under average conditions the amount of fluid so excreted amounts to several hundred cubic centimeters in twenty-four hours and, on a warm day, a workingman may excrete several liters; the solids may amount to several grams. In a sweat bath the secretion may rise to a liter in half an hour. In cases of impaired renal efficiency the skin may take a still more active part in eliminating waste products and the excretion of solids may be so great that crystals of urea and sodium chloride appear on the skin.

In cases of severe chronic nephritis a daily warm or hot bath may be advisable. A bath of about 15 minutes' duration at a temperature of about 105 degrees Fahrenheit is good; after the bath, the pa-

tient should be placed in a warm bed with hot water bottles. A person may lose several pounds by a single bath of this kind. If, after a course of such baths, the patient becomes weak and tired the after-treatment can be omitted first, and later, the duration of the bath can be decreased. Hot air baths and electric light cabinets can also be used. Electric light cabinets are especially useful; they act quickly and the head and face of the patient can be kept comfortably cool with cloths moistened in cold water. In such cases, and those in which the heart is badly affected, caution in the use of very hot baths should be exercised lest the symptoms become aggravated. In any case, to keep the skin clean, the patient should have at least a daily sponge bath with warm water. Wet packs are useful, especially with children: the child is wrapped in a blanket that has been wrung out in hot water and outside this a rubber blanket is rolled; he can be kept an hour a day in such a pack.

Pilocarpin may be used to stimulate the secretion of sweat; it may be given—1/20 to ½ a grain of pilocarpin hydrochloride—when the patient enters the bath. Pilocarpin is considered harmful in cases showing any tendency to pulmonary edema.

A warm, dry equable **climate** is advantageous to patients with nephritis; such a climate promotes excretion through the skin and does not cause undue stimulation of the metabolism.

**Direct removal of fluid.** It is often necessary to resort to direct removal of accumulated fluid. The **peritoneal cavity** may be tapped to relieve ascites; the **pleural cavity** may be tapped when the accumulation of fluid is so great as to interfere seriously

with respiration. In cases accompanied by severe edema of the legs, the **skin may be punctured** with a lance or scarified in several places. Large quantities of fluid can sometimes be removed by inserting a silver cannula (Southey's tube) into the subcutaneous tissue of the thigh.

Fluid and toxic products may be directly removed by **venesection**; a pint or more of blood may be removed. This measure is especially indicated in full-blooded persons with high blood pressure, in those threatened with uremia or cerebral hemorrhage, and in patients with severe edema; in such cases the operation is followed by the hastening of absorption of interstitial fluid and rapid relief of the symptoms. Sometimes, after removal of blood, an equal, or slightly larger quantity of physiological salt solution is introduced into the vein. The normal salt solution introduced is believed to increase the hydremia—that is, the amount of "free" water as compared to the "hydration" water—and, this is probably accompanied by a transfer of some of the crystalloids—both salts and toxic products—from the colloids to the free water making these crystalloids in this way available for excretion. This is the most plausible explanation of the very rapid and extensive diuresis which follows the operation in cases with complete suppression of urine.

### Stimulating Renal Activity.

The kidney may be stimulated to increased activity by diuretics. The potassium and sodium salts of aliphatic acids—potassium citrate, potassium acetate, cream of tartar—oxidize in the body to bicarbonates and act as mild diuretics. The cause of

the diuretic action of these salts is not entirely understood; possibly the bicarbonates formed increase hydremia either because they are difficultly diffusible and, therefore, attract water into the circulation,* or because they neutralize acid products in the colloids and the neutral salts thereby formed, in passing to the "free" water, carry "hydration" water with them, making it "free" and, therefore, available for excretion. The same factors may be responsible for the increased flow of water through the kidneys accompanying the actual excretion of these and other salts. These salts can be given in the form of pleasant-tasting drinks such as lemonade. Another good diuretic drink, made by dissolving a drachm of cream of tartar in a pint of boiling water to which a little lemon juice and sugar have been added, is pleasant when taken cold.

Members of the caffein group, especially caffein, diuretin, and theophyllin, are used as diuretics. The action of these drugs is not due to nervous or vascular effect but to direct stimulant action on the kidney cells themselves. These drugs all have, also, a stimulant action on the central nervous system and this action is antagonistic to their diuretic action; but, except in the case of caffein, this central action is probably rarely effective in completely neutralizing the diuretic action. In the case of caffein, however, as a consequence of this antagonistic central action, the diuretic effect is uncertain and, especially in high-strung, nervous individuals, may fail to appear. An alcoholic drink equivalent to half an ounce to an ounce of whiskey is usually sufficient to overcome this central action of the caffein. It is

* See, however, footnote, page 19.

well to remember that an overdose of these diuretics of the caffein group may have an opposite effect and cause oligurea; furthermore, when these drugs are given for more than a couple of days the diuretic effect does not usually last. One way to administer them is to give three doses (2 grains caffein, 3 grains of theophyllin, or 10 grains of diuretin) in one day, and not repeat for a few days. If the tolerance of the body to one of these drugs increases so that the drug temporarily ceases to be effective as a diuretic, one of the others may be tried for a time.

One drug, not much used, but, nevertheless, very effective as a diuretic is calomel—given sometimes with opium to avoid its laxative effect; it makes the mouth, gums, and teeth very sore and is used only in small doses and then only in desperate cases when other diuretics have proved ineffective. Some pharmacologists attribute the diuretic action of calomel to the irritant action of the mercury ion directly on the kidney cells; other pharmacologists deny this and say that calomel acts like the hydragogue cathartics in attracting water to the intestine; if this water is not quickly excreted it may, later, be reabsorbed; but since, in the mean time, the blood has made up for its depletion by absorption of interstitial fluid, the reabsorption of water from the intestine leads to hydremia and diuresis.

Irritating substances like cubebs and copaiba should not be used as diuretics in cases of nephritis.

If circulatory disturbances are responsible for impaired kidney action, the action may be bettered by improvement in its nutrition; this may be brought about by drugs of the digitalis group which stimulate the heart.

## Other Details of Treatment.

**Good hygiene.** In addition to the methods of treatment already outlined, attention is given to certain details of general hygiene. Alcohol, which may irritate the kidneys, and tobacco, which may damage the heart, should be prohibited, or permitted only in moderation. The circulatory changes which follow chilling have a deleterious effect on the kidneys; and nephritic patients are especially subject to pulmonary disorders; such patients should, therefore, be protected from sudden changes in temperature. If there is anemia, iron may be given but only when there are no acute symptoms.

**Symptomatic treatment.** Dyspnea, nausea, and vomiting are usually relieved only with improvement in the general condition. A comfortable bed rest makes breathing easier; if the dyspnea is due to fluid in the pleural cavity this fluid may be removed by aspiration. For the nausea and vomiting bits of ice or effervescing drinks may be given; the quantity of food may be decreased. Headache and dizziness often accompany the high blood pressure and may often be relieved by nitrites. For pain in the back, or hematuria, warm poultices may be applied to the small of the back.

In the very severe grades of nephritis, symptoms of **uremia** may appear. These symptoms, of unknown origin, but possibly the result of retained waste products, are variable; they affect usually the central nervous system, and the gastro-intestinal tract. The patient may be dull, apathetic or in coma, or may be excited, or even maniacal; he may show disturbances of respiration, and various sensory

and motor disturbances; he may suffer from nausea and vomiting, or diarrhea. The treatment is based on the assumption that it is a toxemia due to retained waste products, and all the most active methods for eliminating waste products discussed in the foregoing paragraphs may be used. For the restlessness, delirium, and convulsions, morphia, or chloral—for severe convulsions, even ether—may be used.

## Forms of Kidney Disease.

The importance of disturbance of function as distinct from anatomical change as a basis for the classification of disease from the standpoint of therapeutics is clearly discernible in the case of kidney disease. In kidney disease, as in heart disease, the indications for treatment depend not so much on the exact character of the pathological lesions and their distribution as on the severity of the functional disturbance; what interests us chiefly is the extent to which the power of excreting the waste products of metabolism is impaired. A knowledge of the amount of albumin, cells, and casts in the urine does not always help us on this point; the extent of such impairment can be judged only by the clinical signs which result from retention of fluid and waste products. Attempts have long been made to measure quantitatively the efficiency of the kidney in excreting waste products, but efforts in this direction have only just begun to be successful; in making such measurements, definite quantities of water, salts, dyestuffs, and nitrogenous food are administered and the amount secreted in a definite time compared with the normal. The principles of treatment are in

all cases those outlined; the details of the methods chosen depend on the severity of the disease—the more severe the disease, the more active the treatment.

The pathologists, possibly, too, the clinicians, have rather overclassified kidney disease; comparison of the findings at autopsy with the clinical diagnosis in a very large series of cases leads to the conclusion that we are scarcely warranted, at present, in dividing Bright's disease into more than three clinical forms at most—acute Bright's disease, and two forms of chronic Bright's disease—and we sometimes fail to distinguish among these three forms. Under acute Bright's disease are included those sudden degenerative changes induced by the diffusible toxins liberated in acute infectious diseases; by certain mineral and organic poisons such as mercury, arsenic, and cantharides; and, sometimes, simply by exposure. One form of chronic nephritis is that often known as parenchymatous or glomerular nephritis; in the earlier stages—acute and subacute—it may be accompanied by marked dropsy, edema, and retention of urine, and the urine may be concentrated, and contain much albumin and abundant form elements; in the later stages the urinary findings may be almost negative. This form of nephritis may follow acute nephritis or come on insidiously. Another form of chronic nephritis is that seen in older people and not accompanied by marked dropsy, associated with an increased rather than a decreased quantity of urine, and with but slight amounts of albumin and form elements; it is a slowly advancing condition often associated with arteriosclerosis, and very marked changes in the kidney may be associated

with apparent good health. Clinically, as well as anatomically, the later stages of both of these forms of chronic nephritis may closely resemble each other.

Attempts are being made to classify on a functional basis; measured amounts of water, salts, nitrogenous foods, sugar, and dyestuffs are administered and the amount excreted in a definite time compared with the normal. This method sometimes, but not often, enables us to recognize types of nephritis in which the power to excrete certain substances and not others is diminished and this may be of therapeutic significance; but, as a rule, these methods serve only as an aid in gauging the severity of the disease.

For the purposes of treatment, nephritis can be most simply divided into mild acute nephritis, mild chronic nephritis, and severe nephritis—acute or chronic.

**Mild acute nephritis.** As in heart disease, so, also, in nephritis, we can, perhaps, speak of preventive treatment for acute nephritis; it is said that a good brisk purgative may sometimes avert a threatened attack of nephritis during scarlet fever or other acute infectious disease.

When examination of the urine following exposure or acute infectious disease gives evidence of nephritis, even though no other evidence of disturbed kidney function is present, the patient should be put to bed and kept warm and quiet and on a strict diet—milk alone, if possible—until all evidence of nephritis has disappeared; if there is no dropsy, edema, or other evidence, except in the urinary findings, that the kidney is not competent to its tasks, more active treatment may not be necessary.

**Mild chronic nephritis.** When examination of a man past middle life shows slightly increased blood pressure, and urinary changes indicative of a beginning chronic nephritis of the arteriosclerotic type, active treatment may not be necessary. The situation should be explained to the patient; he should be enjoined to live a good hygienic life, to avoid excitement, worry, fatigue, and excesses, and to exercise moderation in all things, especially in eating and drinking. Tobacco and alcoholic drinks should be forbidden or restricted. The patient need not give up all muscular work; a certain amount is advisable. He should keep his skin and bowels moderately active. Under such a régime the patient may live a long life free from any marked subjective or objective symptoms.

**Severe nephritis.** With marked subjective and objective signs of a lowered kidney efficiency, either in acute or chronic nephritis, all the various methods of treatment outlined in the preceding paragraphs may be used. Dietetic measures and stimulation of the skin by baths, and of the bowels with cathartics, are always safe to begin with. With more severe grades of disease all the active methods of treatment may be used. Rest in bed and a strict milk diet are not, of course, unless absolutely necessary, as strictly adhered to in chronic, even severe, nephritis as in acute nephritis. The details—when to begin different forms of treatment, choice of methods, size of doses—can be learned only by clinical experience, not from a book.

**Other urinary diseases.** In such inflammatory conditions as **pyelitis, pyelonephritis, renal abscess, perinephritic abscess,** and **cystitis,** the general meth-

ods used in the treatment of Bright's disease, especially dietetic measures and purgation, are employed. To dilute and wash out the infectious material, large quantities of fluid are given to drink. Substances such as sandalwood oil, copaiba, and, especially, hexamethylenamin (urotropin) which are excreted in the urine in the form of antiseptic compounds, are administered. If the urine is strongly acid, dilute alkalies, or the potassium, or sodium salts of the aliphatic acids, which, in the body, change to alkalies, may be given; if the urine is alkaline, benzoic acid, which combines with glycocoll and is excreted as hippuric acid, may be given. When the condition is very severe, the surgeon may be called upon to drain the pus. The pain may be combated by local applications or with hypnotics.

A patient may pass fine sand for a long time without serious trouble; but a **stone** of any considerable size may partly block the ureter and cause great pain. In such a case, the patient should drink freely of warm alkaline drinks to flush out the ureter; hot baths, or atropin, may sometimes relax the spasm of the ureter and permit the stone to pass on. For relief of the pain hot poultices, cloths wrung out in hot water, morphia, atropin, and, when the pain is very severe, chloroform inhalations may be used. Changes of posture occasionally give relief. Surgical interference may be necessary. Alkalies and piperazin, often given as uric acid solvents, are of no value; such stones are rarely urates, usually oxalates; in neither case have alkalies or piperazin any solvent effect. Various dietetic measures recommended as preventing the formation of stones are not known to be effective.

# DISEASES OF THE VESSELS.

The most common forms of disease of the arteries are arteriosclerosis and aneurism.

### Arteriosclerosis.

Arteriosclerosis is only an anticipation of the changes seen in old age; the cause is unknown but the onset is probably hastened by syphilis, by such poisons as lead, alcohol, and tobacco, and by undue bodily and mental strain. It is the signal for a more careful mode of life. In the later stages both the heart and kidney are frequently affected; the kidney shows chronic interstitial nephritis; and, as a result of the increased blood pressure consequent upon the stiffened arteries, the heart shows hypertrophy. As a result of the changes in the arterial walls, vasomotor response to regulate the rapid changes in blood supply needed by different organs becomes impaired, and the nutrition of the various organs and of the body as a whole suffers. The patient responds badly to the various muscular, metabolic, and mental stresses and strains of life, and cannot stand exertion of any kind so well; the excretion of the waste products of metabolism becomes impaired.

The general methods of treatment are based on the same principles as those used in other forms of chronic functional inefficiency. In order that the demands upon the various organs shall not exceed their powers; in order to maintain the equilibrium between the work required and the work which can

be done, stresses, strains, exertions, demands of all kinds on the activity of the various affected organs are decreased, and, at the same time, the organs are stimulated: this applies especially to the kidneys, heart, vessels, and gastro-intestinal tract. In the early stages, when no marked symptoms are present, the condition should be explained to the patient, and he should be enjoined to live a good, quiet life free from excesses of all sorts especially in eating and drinking; he should use little or no alcohol or tobacco, keep his skin and bowels active, and protect himself from sudden changes of temperature. His diet should be light and easily digested; not enough food should be taken to cause increase in weight; plethoric patients may even lose weight. Meat, especially, should be used only in moderation—once a day is enough. Great excitement is accompanied by an increase in the force of the heart beat and an increase in the contraction of the smaller arteries, changes which increase the blood pressure; excitement, worry, and all forms of excessive mental activity are, therefore, especially harmful and should be avoided. Irregularity of the pulse, nervousness, sleeplessness, and loss of appetite are indications of over-exertion of some kind. The blood pressure, especially, should be watched, and, by the use of nitrites, massage, hydrotherapy and other measures, kept from rising too high; sudden alterations in blood pressure, particularly sudden increase, should be avoided. In syphilitic patients mercury, potassium iodide, and salvarsan may be used.

Later, if symptoms of failure of compensation of the heart or kidneys appear, all the different methods of treating diseases of the heart and kidneys

may be used. The high blood pressure of arteriosclerosis is not necessarily a contraindication to the use of digitalis. Such high blood pressure is generally attributed to toxic products of metabolism present in increased amounts resulting from imperfect excretion; with the improvement in circulation following the use of digitalis even a fall of blood pressure may follow.

## Aneurism.

The treatment of aneurism is similar to that of arteriosclerosis; the same precautions against excesses of all kinds are observed. All forms of exertion and excitement tend to increase the heart rate and the subjective symptoms; patients with aneurism should, therefore, be kept quiet—if possible, in bed. A very low diet for a long period, especially one very poor in liquids, has been recommended; it is said to reduce the blood volume and render the blood more fibrinous and to be followed by good clinical results. Attempts are sometimes made to obliterate the sac by inducing clotting of the blood in it; long wires are introduced by the surgeon and an electric current passed through the wires. If the blood pressure is high, nitrites may be given; venesection may sometimes prove helpful. To relieve the pain local application, such as an ice-cap, or hypnotics like morphine may sometimes be necessary; potassium iodide is especially useful and is believed by many to have, besides, some effect in diminishing the size of the sac.

# DISEASES OF RESPIRATION.

Respiration is the exchange of oxygen and carbonic acid between the external air and the tissues. The activity of the metabolism determines the amount of oxygen needed and the quantity of carbon dioxide formed. The exact details of the process are not fully understood; but the metabolic changes affect the composition of the blood, and when the carbon dioxide content of the blood—or, perhaps, more accurately, the acidity of the blood—reaching the respiratory centre increases and the oxygen content decreases, inspiration is stimulated. The respiration is regulated, therefore, by the metabolism and not the metabolism by the respiration. Ordinarily, inspiration, only, is the active process, expiration being purely passive; but in dyspneic patients expiration, too, may become active. Every increase in metabolism leads to an increase in the carbon dioxide content and a decrease in the oxygen content of the blood, and when this blood reaches the respiratory centre respiration is stimulated; there is a prompt response to the needs of the metabolism.

Respiration may be divided into four parts:

(a) The exchange between the outside air and the alveolar air.

(b) The exchange between the alveolar air and the blood.

(c) The transport of oxygen and carbonic acid by the blood, and

(d) The exchange of oxygen and carbonic acid between the blood in the capillaries and the tissues.

The first two parts are referred to as external respiration, the last two as internal respiration.

Any condition which interferes with the exchange of oxygen between the external air and the blood, with the transport of oxygen or carbon dioxide, or the exchange between the blood and tissues, may affect respiration. Examples of the disturbance of external respiration are seen in pneumonia and in pulmonary tuberculosis, conditions in which the capacity of the lungs is decreased, and in emphysema in which, as a result of excessive expansion and coalescence of alveoli, there is a decrease in the surface exposed to aeration. Examples of disturbance of transportation are seen in anemia, in diabetic acidosis, and in diseases of the heart and kidneys; in anemia, the power to transport oxygen is decreased; in diabetic acidosis the power to transport carbon dioxide; and as a result of the congestion in diseases of the heart and kidneys neither oxygen nor carbon dioxide are properly transported. Conditions such as anemia and diabetic coma, in which there is interference with the transport of oxygen and carbon dioxide, are discussed elsewhere; only diseases of external respiration are discussed here.

## Principles of Treatment.

In the discussion of treatment of diseases of the heart and kidneys it was pointed out that the most important factor is not the nature of the anatomical change but the degree to which function is dis-

turbed. Though this fact, because of being obscured by certain complicating factors, is less evident at first in the case of diseases of the lungs, it is, nevertheless, true also for such diseases. One reason for an apparent difference in the principles of treatment lies in the fact that whereas a great proportion of the patients with diseases of the heart, kidney, and vessels are suffering from chronic degenerative changes, the greater proportion of all patients with diseases of respiration are suffering from infectious diseases such as pneumonia and phthisis, and, as already pointed out, infectious disease is treated on somewhat different principles from the usual chronic diseases. A more important reason for the apparent difference is that it is possible to treat separately the different elements involved in diseases of respiration somewhat more successfully than the elements involved in disturbances of the circulation of the blood or of secretion through the kidneys. In the case of the chronic nephropathies the exact anatomical nature of the process is of far less significance from the standpoint of therapeutics than the severity of the disease as measured by the degree of functional inefficiency; and in the case of heart disease, though the details of treatment may be modified by the nature and distribution of the lesions, the general principles depend chiefly on the degree of efficiency of the circulation. Disturbances of respiration, on the other hand, may be due to several different factors, all of which may be treated separately as:

(1) Conditions outside the lung, either in the upper air passages or in the chest wall—nasal polypi, adenoids, enlarged tonsils, rhinitis, a

diphtheritic exudate, deformities of the spine, lessened elasticity of the ribs.

(2) Congestion in the lung secondary to heart or kidney disease.

(3) Disease in the pleura, or

(4) Disease of the lung itself.

In the lung itself there may be an exudate in the air spaces of the alveoli, or the condition may affect the circulation, the elastic fibres, the unstriped muscles, or the mucous membranes. These different elements involved may be treated separately with more success than the different elements involved in diseases of the heart and kidneys. We can increase or decrease the rate or depth of inspiration or expiration or the activity of the circulation or the condition of the muscle fibres, the elastic fibres, or the mucous membranes; respiration may be affected by bringing influences to bear on the heart, on the blood, on the kidneys, on the respiratory centre, on the muscles of the chest wall, or the unstriped muscles in the lung, on the elastic fibres, on the mucous membranes, or on the general metabolism. The successful treatment of diseases of respiration depends on a careful diagnosis of the nature of the disturbance and a knowledge of methods of influencing the different factors involved in the process of respiration. We can, and do, at times, stimulate respiration as a whole by climatic treatment—high altitudes, cold, dry air—by cold baths, exercise, improvement in the nutrition by dietetic measures, stimulants for the gastro-intestinal tract, and heart tonics, and we can, and do, decrease respiration by rest in bed, by moderation in using the voice, by living in a warm, moist climate at sea-level, and by hypnotic drugs

which decrease reflex irritability. Respiration may, furthermore, be decreased in one part of a lung by immobilization of the muscles of the chest wall with a tight bandage or strips of adhesive plaster. Aeration of the whole lung or parts of the lung may be increased by suitable postures and exercises. But the different factors concerned in the function of respiration are better open to direct treatment than are the factors in diseases of the heart and kidneys so that we more often stimulate or rest the respiratory centre, the circulation in the lung, the mucous membranes, the elastic fibres, the unstriped muscles, or the pleura alone than respiration as a whole.

**Influencing the respiratory centre.** Through stimulation of the skin by means of friction and applications of cold water or ice, the respiratory centre itself may be affected. In unconscious patients, with shallow breathing, the respiration may be increased and the patient brought back to consciousness by applications of ice to the region of the spine or the medulla. The respiratory centre may be stimulated directly by caffein, atropin, or camphor, and, according to many investigators, by alcoholic drinks; indirectly through stimulation of the trigeminal and olfactory nerves by means of various volatile substances—ammonium carbonate (smelling salts), and vinegar.

Increased respiration due to nervousness may be depressed by hypnotics of the morphine group—morphine, codein, heroin, dionin. Heroin is especially depressing on the respiratory centre and for this reason, especially in the case of children and patients with pneumonia, should be administered with great caution. Morphine renders the centre less sensitive

to excitation and, as a result, makes respiration slower, deeper, and quieter—somewhat as digitalis makes the heart fill itself more slowly and more completely—and so, therefore, often spares the strength of a patient with rapid and shallow respiration.

Respiration is affected also by altitude: inspiration is prolonged and expiration shortened by the rarefied air at high altitudes; during the prolonged inspiration more blood passes through the lung and the lung is better nourished.

**Improvement in the circulation and blood.** Respiration in the lungs may be bettered by improving the circulation. The marked congestion of the lungs accompanying severe heart disease and kidney disease is treated not as a disease of the lungs but as a disease of the heart or kidneys. The stagnant circulation in the lungs accompanying typhoid and other fevers necessitating long-continued rest in bed may be improved by application of cold and friction to the chest wall. The nutrition of the lung itself is promoted not only with improvement in the rate of blood flow but also with improvement in the blood itself; anemia and all forms of malnutrition should therefore be treated. The efficacy of the cold air treatment of tuberculosis is to be attributed partly to the improved nutrition of the lungs resulting from the increase in the metabolism.

**The unstriped muscles.** Bronchial asthma is believed to be due to spasm of the unstriped bronchial muscles. To combat this spasm drugs of the atropin group are used—atropin, hyoscyamus, stramonium, lobelin. These drugs paralyze nerve endings in unstriped muscles and cause the muscles to re-

lax. They are sometimes administered in the form of cigarettes made of the leaves of plants containing these alkaloids dipped in potassium nitrate; or the leaves are burned in a saucer and the smoke inhaled. Inhalation of fumes of ammonia or of amyl nitrite sometimes helps. Epinephrin also causes relaxation of bronchial muscles and is often effective. Filling the patient's room with steam, and various forms of hydrotherapy, especially hot foot baths, often give relief. Potassium iodide, and wine of ipecac sometimes make the attacks less frequent. Obstruction somewhere in the respiratory tract, and gastro-intestinal, or genito-urinary disturbances are sometimes responsible for the condition; these, and any other pathological condition should always be treated. Bronchial asthma is very difficult to alleviate; sometimes all the methods at our disposal fail to help and even after we find something apparently helpful at first its effectiveness often disappears on continued use.

**The elastic fibres.** Ordinarily, inspiration, only, is an active process; expiration is passive—due in part to the contraction of the elastic fibres. If the elasticity of these fibres is destroyed, the lung does not contract sufficiently on expiration; the alveoli become expanded and their volume changes but little on each complete breath; the alveoli may then coalesce and so bring about emphysema. Such a condition is sometimes seen in those with asthma and in persons such as glass blowers whose lungs are constantly overdistended. Attempts are made to influence the elastic fibres by the use of compressed air cabinet, rarefied air cabinets, by forced expiration exercises, and by blowing bottles.

**The mucous membranes.** For facilitating the work of the mucous membranes and preventing undue irritation pure air free from dust and containing a certain amount of moisture is best. The temperature of the air has probably little direct influence on the mucous membranes; the air becomes warmed before reaching the deeper parts. Air containing dust causes irritation and predisposes to pulmonary troubles; inhalers are sometimes necessary for protection of persons working at very dusty trades. The amount of moisture in the air is probably important; dry air becomes charged with moisture in the upper air passages during inspiration but very dry air causes irritation to these parts. The catarrhal condition of the upper air passages so common in the hot, dry rooms of our modern steam-heated houses during the winter is often promptly relieved by charging the air with moisture, or by a sea trip. Various drugs are used in the treatment of disorders of the respiratory mucous membranes. Creosote is used by some physicians who believe that it is excreted in part through the respiratory mucous membranes and there acts as an antiseptic. Other drugs are used to soften and facilitate expectoration; among these are members of the sodium chloride group—sodium chloride, potassium iodide, potassium sulphocyanate—the alkali group, ammonium salts, pilocarpin, senna, and small doses of emetics—apomorphine, and tartar emetic. In spite of much investigation the mode of action of these substances is not yet entirely clear.

**Symptomatic treatment.** The pain of pleurisy may sometimes be relieved by painting the skin over the affected area with tincture of iodine

or by strapping the affected side with a tight bandage of adhesive plaster. The severe pain in pneumonia may be diminished by local application of ice or by hot water bottles and by various hypnotics, especially morphine.

**Cough** is not always treated in the same way under different circumstances. Many forms of milder cough such as that in chronic phthisis are best left without direct treatment. A troublesome cough may be relieved by morphin, codein, heroin, or dionin; codein, especially, is effective, is not a habit-forming drug like morphin, and does not depress the respiratory centre so severely as heroin. It is better not to give codein or morphin when expiration is difficult and tenacious; these drugs make the bronchial secretion less watery. If gastro-intestinal disturbances, nervous disorders, or irritation of the upper air passages are responsible for the cough, those conditions should be treated. In the case of the cough of broncho-pneumonia in children we try to assist the efforts made to expel mucus from the respiratory tract.

## Different Diseases of Respiration.

**Bronchitis.** Chronic bronchitis often accompanies other chronic diseases of the lung, Bright's disease, heart disease, gout, arteriosclerosis, and aneurism of the aorta. The accompanying chronic disease is treated and the patient protected as much as possible from exposure and sudden changes—advised to live in a warm, equable climate if he can.

Acute bronchitis and coryza are treated by empirical methods. The patient is given hot drinks, a hot foot bath, and Dover's powder; he is wrapped

up warm in bed to promote sweating, and care is taken to keep the air of the room warm and charged with moisture. Many other methods of treatment are in use and will be found described in the text books.

**Bronchial asthma.** Bronchial asthma is generally attributed to spasm of the bronchial muscles accompanied by swelling and hyperemia of the mucosa; these changes explain the hindrance to inspiration and expiration. The attack may be due to a variety of causes; in most cases there is a strong neurotic element. Sometimes, as in the form of asthma due to irritation of the mucous membranes by the pollen of certain plants, and by certain articles of food, measures may be taken to avoid the irritating influences. Atropin and other members of the atropin group—stramonium, lobelin, hyoscyamus —or epinephrin, all of which paralyze nerve endings in the bronchial muscles and cause relaxation, may be given; hot alcoholic drinks, morphia, inhalations of chloroform—which decrease reflex irritability— and many other drugs—amyl nitrate, pilocarpin, cigarettes to which potassium nitrate has been added, or cigarettes made from plants rich in potassium nitrate—have been used during attacks. Attacks may sometimes be warded off by the use of potassium iodide, epinephrin, or wine of ipecac.

**Pleurisy.** If there is little or no effusion, the pain of pleurisy may be relieved by counter irritants or by strapping the side. Pleurisy with effusion is treated in a somewhat similar manner to pericarditis with effusion; the patient is kept at rest in bed, on a diet poor in liquids, and elimination of water through the bowels, skin, and kidneys is promoted

by cathartics, diaphoretics, and diuretics. When the effusion persists for weeks or is very extensive or is the cause of very marked pressure symptoms thoracocentesis should be done. Since in cases of hemorrhagic effusion or those which are the result of carcinoma the pleural cavity, as a rule, promptly fills up again, tapping is best not done in such cases. In cases of purulent effusion, gangrene, or abscess, surgical interference may be necessary.

# DISEASES OF THE BLOOD.

## Anemia.

Anemia results in a disturbance of internal respiration whereby, as a consequence of a decrease in the amount of hemoglobin, or in the number of red cells, there is a diminution in the power of the blood to transport oxygen. The nutrition suffers, the patient loses strength, and is easily tired. The striking feature may be, as in chlorosis, the decrease in the amount of hemoglobin in the corpuscles, or, as in pernicious anemia, a decrease in the number of corpuscles per cubic millimeter of blood. In any case, the anemia must be due to a loss of equilibrium between formation and destruction of red cells or of hemoglobin; when the rate of destruction exceeds the rate of formation either the number of red cells or the amount of hemoglobin decreases. The treatment aims at decreasing the excessive destruction and increasing the formation of hemoglobin and red cells. We see occasionally cases of anemia due to a decrease in the rate of formation of blood corpuscles; in such cases there is, not hyperplasia of the bone marrow and hemopoietic centres, but hypoplasia. Anemia is usually, however, the result of an increase in the rate of destruction of red cells; such cases are further classified into primary and secondary anemia.

The classification of anemia into primary and secondary forms, while not strictly scientific, since all forms of anemia are secondary to some more fun-

damental disturbance—known or unknown—is, nevertheless, useful and important from a therapeutic standpoint, since in secondary anemia the cause of the disorder may be recognized and combated. Secondary anemia may be due to:

(a) A loss of blood, either a single large loss, or repeated smaller bleedings (ulcer of the stomach, hemorrhoids).

(b) Prolonged loss of albuminous material (long continued diarrhea, Bright's disease, prolonged lactation).

(c) Constitutional disease such as syphilis, tuberculosis, cancer, myxoedema, and chronic constipation.

(d) Absorption of poisons such as lead, mercury, and the poison of intestinal parasites; or even to

(e) Bad hygiene and improper food.

In primary anemia the cause is unknown.

In all forms of anemia, iron compounds should be tried. It is not so very long since it was believed that organic iron compounds are the only effective iron compounds; it was admitted later that inorganic iron is equally effective; at present inorganic iron is believed to be more effective. The mode of action of iron is not entirely understood. It is not now generally believed that the iron acts simply as a rich supply from which hemoglobin can be formed; if this were the mode of action, the various forms of food which contain organically combined iron would be equally as effective as inorganic iron. There is experimental evidence to indicate that inorganic iron causes active stimulation of the process of formation of red blood corpuscles. Iron, therefore, may serve not

only as a source for formation of hemoglobin, but may also cause increased formation of red blood cells. Some pharmacologists still deny that inorganic iron either specifically stimulates hemoglobin formation or even serves as a source from which hemoglobin can be formed; they ascribe its effectiveness in anemia simply to improvement in absorption resulting from the stimulating and irritating action of the iron salts on the walls of the gastro-intestinal tract. Iron carbonate in the form of Blaud's pills is much used; the first week usually one pill three times a day is given; the second week, two pills; the third week, three, and the treatment is kept up a month or more. If there is diarrhea, the iron carbonate, which is a mild astringent, may serve to diminish this; if there is constipation iron, combined in organic form, ferratin, for example, is sometimes used. It is well to remember that many foodstuffs—beefsteak and certain vegetables like spinach—contain iron in a form easy to assimilate.

Next in value to iron is arsenic. This element, which has long been used to improve the nutrition of cattle, leads to better assimilation of food, deposition of fat and gain in weight. How it acts is not entirely clear; the action is generally attributed to improvement in absorption resulting from dilatation of splanchnic vessels. Given as sodium arsenite in the form of Fowler's solution, it is administered in doses of gradually increasing size, beginning with 3 minims three times a day and gradually increasing up to fifteen or twenty minims three times a day.

The anemia following loss of blood is sometimes treated by injections of normal salt solution; the salt solution may be introduced into the rectum, or

given subcutaneously, intraperitoneally, or intravenously, the methods depending on the urgency of the case. All forms of anemia have been treated by transfusion of blood from a healthy person. In all forms of anemia good hygiene is important. The patient should be allowed sufficient rest, kept in the open, and given plenty of good, nourishing food. It is of the utmost importance to keep the bowels active; in chlorosis, cathartics act sometimes almost as a specific. Rest, too, is important since all muscular activity is accompanied by the destruction of red cells.

In cases of primary anemia which are not of the aplastic type—that is, cases due to increased destruction of red cells rather than decreased formation—splenectomy is sometimes followed by good results. These two forms can be differentiated by a determination of the urobilin in the stools; urobilin is derived from the bile pigments and these, in turn, from hemoglobin so that an increase in urobilin indicates increased destruction of red cells. Splenectomy is believed to remove the organ chiefly responsible for the increased hemolysis in such cases.

### Leukemia.

Nothing but good hygiene—fresh air, good food, and freedom from care—seems to have any effect in leukemia. Arsenic, iron, and x-ray treatment are used but the results are doubtful. Benzol is sometimes administered but, although it decreases the number of leucocytes, it is, nevertheless, unsafe to use on account of the danger of fatal results. On account of the many remissions, even without treatment, in this disease, the effect of treatment is difficult to gauge.

# DISEASES OF THE GASTRO-INTESTINAL TRACT.

## Physiological Part.

Though the number of diseases of the gastro-intestinal tract successfully treated by direct, surgical methods is constantly increasing, the greater number of such diseases is still treated by the indirect methods of the physician, that is, by methods directed at the functions rather than the structure of the tract; the two great principles made use of in the treatment of diseases of the heart, kidneys, and lungs—namely, rest of function, and stimulation of function, are used. It was pointed out that in the case of disorders of the heart and kidneys the significant feature in therapeutic classification is the **severity** of the disease, the **degree** of functional disturbance. In the case, too, of diseases of the gastro-intestinal tract, it is true that the degree of functional disturbance is of the utmost importance, but since the gastro-intestinal tract is made up of different parts and each part has several functions—motor, secretory, digestive, absorptive—disease of these different parts and functions can be treated separately and by different methods so that it is important to recognize which part and which function is diseased; in other words, diagnostic skill in recognizing the exact nature of the disturbance becomes of the utmost importance.

A recognition of the nature of the disturbance, and an intelligent application of the proper treat-

ment in gastro-intestinal disease, depends so directly on a knowledge of the physiology of digestion, that diagnosis, rational treatment, and physiology are best discussed together. The best introduction to the general principles of the practical therapeutics of gastro-intestinal diseases consists in a properly selected statement—a statement in which emphasis is laid only on the features of practical significance as we now understand them—of the physiology of the gastro-intestinal tract, together with a brief account of the methods of influencing the many functions of the tract. The manifestations of gastro-intestinal disease are so varied in their nature and intensity in different cases that the way in which physiological and pharmacological knowledge is to be applied depends very much on the individual case; the treatment of diseases of the gastro-intestinal tract is one of the best examples of the great importance to the physician of a combination of fundamental scientific knowledge of physiology together with the cumulative experience that is acquired as the result of long clinical observation; there is no group of diseases in which individualization of treatment is more important than in those of the gastro-intestinal tract.

## Functions of the Gastro-Intestinal Tract.

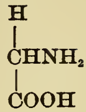
Until comparatively recently the complex compounds which make up the greater part of our foodstuffs—protein, fats, and carbohydrates—were believed to be synthesized under the influence of sunlight in plants and then after very slight chemical change, absorbed and utilized in the animal body. We now know that this is not correct and that, on

the contrary, foodstuffs are absorbed from the gastro-intestinal tract only after they are split to very simple compounds. If albumins or complex carbohydrates are injected into the blood they are not utilized but are excreted unchanged through the kidneys. It is the function of the gastro-intestinal tract to take complex foodstuffs received in a great variety of physical and chemical forms and split them up into a limited number of comparatively simple compounds which the tissue can utilize. Proteins are split to the simple amino acids of which they are constituted; carbohydrates to simple monosaccharides; fats to fatty acid and glycerin. These amino acids, monosaccharides, and fatty acids are then in part utilized to give energy to the body and in part recombined to form the proteins, fats, and carbohydrates characteristic of man and differing somewhat in structure from the compounds from which they were originally derived. This is not the place to go into the chemistry of the foodstuffs, but on account of the necessity of referring to the therapeutic bearing of some of the more recent work, a very brief reference to certain features of protein chemistry is unavoidable.

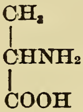
On hydrolyzing proteins with strong acids, or on splitting them with digestive enzymes a limited number, less than a score, of end products is formed. They are all acids, contain nitrogen, usually in the form of an amine group ($NH_2$), and have the general formula:

$$\begin{array}{l} \mathrm{R} \\ | \\ \mathrm{CH} \cdot \mathrm{NH_2} \\ | \\ \mathrm{COOH} \end{array}$$

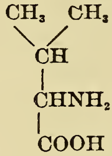
The simplest is glycocoll:



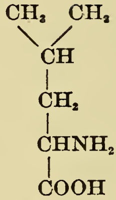
Others of the aliphatic series are:



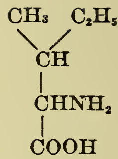
Alanin



Valin

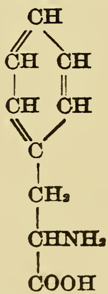


Leucin

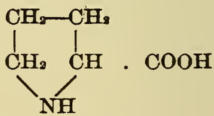


Isoleucin

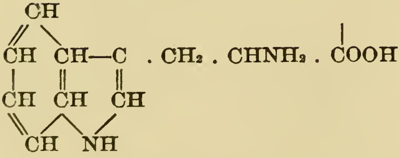
Of the ring compounds may be mentioned:



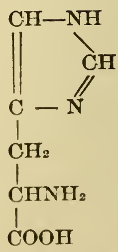
Phenyl Alanin



Prolin

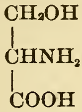


Tryptophan

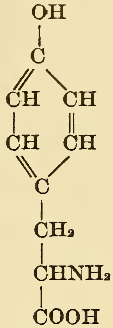


Histidin

The hydroxy derivatives of some of these compounds are also present, thus:



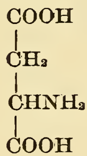
SERIN
(hydroxy alanin)



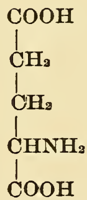
TYROSIN
(hydroxy phenylalanin)

and OXYPROLIN

There are two dibasic acids:

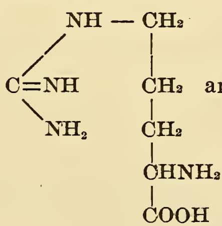


and

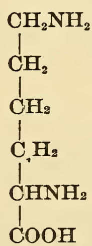


ASPARTIC ACID GLUTAMIC ACID

and two diamino acids:



and



ARGININ LYSIN

One sulphur compound is found, namely, cystin:

$$\begin{array}{lcl} CH_2 . S & . & S . CH_2 \\ | & & | \\ CHNH_2 & & CHNH_2 \\ | & & | \\ COOH & & COOH \end{array}$$

The amounts of these substances in different proteins vary; some of them are even missing from certain proteins. The following table gives a general idea of the percentage composition of a few well known proteins in amino acids:

| | Egg Albumin | Serum Albumin | Serum Globulin | Casein | Gluten |
|---|---|---|---|---|---|
| Glycocoll ....... | 0 | 0 | 3.5 | 0 | 0.9 |
| Alanin ......... | 8.1 | 2.7 | 2.2 | 0.9 | 4.65 |
| Valin .......... | ... | ... | present | 1.0 | 0.24 |
| Leucin ......... | 7.1 | 20.0 | 18.7 | 10.5 | 6.0 |
| Serin .......... | ... | 0.6 | ... | 0.23 | 0.74 |
| Cystin ......... | 0.2 | 2.3 | 0.7 | 0.065 | 0.02 |
| Aspartic acid .. | 1.5 | 3.1 | 2.5 | 1.2 | 0.9 |
| Glutamic acid .. | 8.0 | 7.7 | 8.5 | 11.0 | 23.4 |
| Lysin .......... | 2.15 | ... | ... | 5.8 | 1.9 |
| Arginin ........ | 2.14 | ... | ... | 4.84 | 4.7 |
| Phenylalanin ... | 4.4 | 3.1 | 3.8 | 3.2 | 2.0 |
| Tyrosin ........ | 1.1 | 2.1 | 2.5 | 4.5 | 4.25 |
| Prolin .......... | 2.25 | 1.0 | 2.8 | 3.1 | 4.2 |
| Oxyprolin ...... | | | ... | 0.25 | |
| Tryptophan ..... | present | present | present | 1.5 | present |
| Histidin ....... | | | ... | 2.59 | 1.76 |

The amino group ($NH_2$) and the carboxyl group (COOH) unite as follows:

$$—CO\boxed{OH + H}NH— \rightarrow —CONH + H_2O$$

The simplest example is given by the combination of two glycocoll molecules:

$$NH_2CH_2CO\boxed{OH + H}NHCH_2COOH \rightarrow$$
$$NH_2CH_2CONHCH_2COOH + H_2O$$

Many such products have been synthesized in the laboratory; they are called peptids—polypeptids, dipeptids, tripeptids, etc.: one with eighteen amino acids has been synthesized. These artificial peptids are believed to have the same general composition as the peptones and the proteins. To such compounds the general formula

$$\begin{array}{ccccccc} \text{—CONH —} & \text{CH} & \text{— CONH —} & \text{CH} & \text{— CONH —} & \text{CH} & \text{— CONH—} \\ & | & & | & & | & \\ & \text{R}' & & \text{R}'' & & \text{R}''' & \end{array}$$

is given; the group represented by R depends on the particular amino acid present.

The process which goes on when protein of the food—say, beef protein—is broken down in the intestine into its amino acids, and then these amino acids regrouped in new combinations to form the proteins peculiar to man, may be roughly compared to the process of tearing down one building—say, a schoolhouse—and utilizing the bricks and other building stones of which it was formed to construct another building—say, a theatre. This process of digestion and absorption takes place chiefly in the small intestine. What goes on in the mouth and stomach is preliminary mechanical and chemical preparation; what goes on in the large intestine is supplementary to the main work of digestion and absorption.

**In the mouth.** In the mouth the food undergoes a certain amount of mechanical subdivision and some slight chemical change; the ptyalin in the saliva acts on boiled starch and changes it to the various dextrines and maltose. No general rule can be given for the amount of mastication necessary; the fol-

lowers of Fletcher undoubtedly exaggerate its importance. Lumps of unchewed food do not pass into the duodenum until they are digested to a thin porridge-like consistency in the stomach, and experiment shows that the amount of unutilized food material in the feces is, as a rule, but little affected by the amount of mastication. Under certain circumstances, on the other hand, bolting the food may be followed by serious consequences; if digestion in the stomach is retarded and time is thereby given for bacteria to act on the food, putrefaction may more easily set in.

**In the stomach.** Although digestion takes place chiefly in the small intestine, the small intestine seems to act best when it receives small quantities of material at a time in the form of a thin, semi-fluid, semi-digested mixture; it is the function of the stomach to prepare this semi-fluid, semi-digested mixture and to act then as a food reservoir from which small quantities of this mixture can be injected into the duodenum from time to time. The preparation has to do largely with dissolving interstitial tissue, setting free cellular material and fat, and bringing about the first stages of the splitting of complex proteins. Carnivorous animals eat a comparatively small bulk of food and the kind of food they eat requires but little preliminary preparation; they have, consequently, a small and simple stomach. Herbivora eat large quantities of food containing much intercellular substance and have, therefore, a large and complex stomach.

Pepsin and hydrochloric acid are secreted in the stomach; pepsin alone is not active but becomes activated by the acid. The pepsin hydrochloric acid

has the property of dissolving and swelling **protein** and partly digesting it to simpler digestive products. These partly digested products are more easily acted upon by the digestive juices of the small intestine. How far splitting into simpler substances ordinarily goes during gastric digestion is not definitely known. In general, the first stages of protein digestion take place in the stomach, the later stages in the intestine. The compound proteins are hydrolyzed in the stomach: hemoglobin, for example, is split to hematin and globin; nucleoprotein to nuclein and simple protein. The gastric juice has also the property of precipitating casein from milk. This action is attributed to the enzyme chymosin (rennin); the purpose of making casein insoluble is believed to be that of holding it back in the stomach until it has become partly digested. Other investigators believe that the insoluble casein which precipitates in the stomach is simply the insoluble calcium compound of the first product resulting from the digestion of caseinogen by pepsin hydrochloric acid, and that rennin is only pepsin.

The **carbohydrates** undergo some digestion in the stomach; in the cardiac end of the stomach, before the contents have become acid, the action of ptyalin continues and a certain amount of dextrin and maltose is formed from the starch. We may speak here also of the effect of the hydrochloric acid of the stomach in dissolving the protein (gluten) of bread, and in this way setting the starch granules free. The process of partial destruction and digestion of the vegetable intercellular binding substances—a necessary preliminary to the setting free of foodstuffs in vegetable cells—takes place partly in the

stomach. The intercellular pectin cannot be dissolved by either the hydrochloric acid or by intestinal digestion alone but only by intestinal digestion after preliminary partial solution by hydrochloric acid; cooking, too, helps dissolve the pectin.

A gastric **fat-splitting** enzyme has been described but it is of little practical significance so far as we know. The solution and partial digestion of protein, especially of connective tissue, in the stomach sets free the fats from the cells of the food; these fats are melted by the heat of the body and distributed in the form of a coarse emulsion by the movements of the stomach, a greater surface being thereby exposed to the action of the intestinal juices. The importance of this melting of the fats is shown by the fact that when pure tri-stearin—a fat with a high melting-point—is fed, about 97 per cent. is found unabsorbed in the feces.

There is very little **absorption** from the stomach; it has been shown that small amounts of peptone and glucose can be absorbed from concentrated solutions of these substances in the stomach, but it is probable that normally such absorption is not of much significance.

The stomach has also certain **motor functions**; contractions pass over the pyloric end of the stomach and, from time to time, the pylorus opens and small quantities of properly prepared food are injected into the duodenum. As soon as a small quantity of the acid stomach contents reaches the duodenum, contact of the acid with the wall of the duodenum leads to closure of the pylorus; the pylorus does not open again to permit more food to leave the stomach until this acid has become

neutralized. The length of time the food remains in the stomach varies in different persons, and varies also with the food—carbohydrates remain the shortest time, fats the longest; it varies also with the amount of hydrochloric acid secretion.

Another function of the stomach is that of **antisepsis**; by virtue of its hydrochloric acid content, many bacteria, especially pathogenic forms, are destroyed by the gastric juice.

The stomach, then, has digestive, motor, storage, and antiseptic functions, and any of these functions may be the subject of disease. The stomach is not, however, an absolutely necessary organ; it has been removed without fatal, or, so far as could be ascertained, distinctly dangerous consequences.

**Functions of the intestine.** The greater part of digestion and absorption takes place in the small intestine; there the carbohydrates are split to simple monosaccharides, fats to glycerin and fatty acid, and proteins to the simple amino acids; and there the monosaccharides, glycerin, fatty acids, and amino acids are absorbed. Digestion in the small intestine goes on under the influence of three secretions—the secretions of the pancreas, the small intestine, and the liver. The pancreatic secretion contains **trypsin**, which acts upon proteins, **amylopsin**, which acts upon carbohydrates, **steapsin**, which acts upon fats, and alkali, which serves to maintain the most favorable medium for the action of the pancreatic enzymes. The secretion of the intestinal wall contains **enterokinase** which, as explained below, acts in conjunction with trypsin, the proteolytic enzyme of the pancreas; **erepsin**, which brings about the final stages of the splitting of protein to amino

acids; and **maltase, lactase,** and **invertase** which split maltose, lactose, and cane sugar, respectively, to monosaccharides.

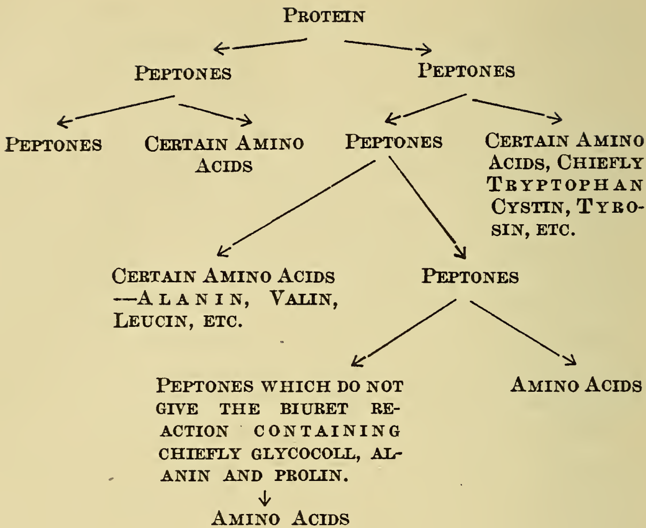
The views regarding the nature of protein digestion have undergone marked and rapid change in the last few years. Until very recently protein was believed to be split into various proteoses (albumoses) and peptones by digestive ferments; the various proteoses and peptones were given various names—heteroproteose, protoproteose, dysproteose, deuteroproteose, synproteose, amphopeptone, antipeptone, and hemipeptone—and were classified into primary and secondary products according to their precipitability with various salts. Precipitability by salts was believed to be determined by the size and complexity of the molecule, the larger and more complex the molecule the greater the ease of precipitation. Tests seemed to indicate that the process of digestion consists in splitting the proteins to molecules of gradually decreasing size and complexity according to a scheme that may be indicated somewhat as follows:

PROTEIN
↓
PRIMARY PROTEOSE
↓
SECONDARY PROTEOSE
↓
AMPHOPEPTONE
↓
ANTIPEPTONE HEMIPEPTONE

The digestive products were believed to be absorbed as proteoses and peptones. Proteoses and peptones, however, were never found in the blood, and when injected acted as poisons and were at once excreted. But this was explained by assuming that

these products are resynthesized to proteins on passing through the cells of the intestine on the way to the blood. It was a search of the mucous membrane of the intestine for the enzyme responsible for this synthesis that gave the clue to the correct solution of the problem: no such enzyme was found; instead, an enzyme, erepsin, was found which splits the peptones further into the simple amino acids of which the proteins are made up. Hundreds of investigations along these lines followed each other in rapid succession until now we have a fairly clear idea of what takes place during intestinal digestion. The terms "proteose" and "albumose" have been dropped as having no significance, and all the digestive products more complex than the amino acids are called peptones. The precipitability of a substance by ammonium sulphate in half or in full saturation—formerly supposed to be significant in determining the molecular size or complexity of the "albumoses"—depends not on molecular size or complexity but simply on the nature of the amino acids in the compound and the particular arrangement of these amino acids. The presence of tryptophan, cystin, and tyrosin in the molecule increases its precipitability by salts.

The picture we now form of protein digestion is shown by the following scheme:




Both large and small molecules are split off from the very beginning. Tryptophan, cystin, and tyrosin are split off early in digestion; this explains why easily salted out compounds—"albumoses"—disappear as digestion proceeds. Glycocoll, alanin, and prolin are split off only late in digestion. The chief part of the digestion takes place under the influence of trypsin; the trypsin is not secreted by the pancreas in active form but as an inactive trypsinogen and is activated by enterokinase. The earlier part of the digestive process takes place under the influence of pepsin hydrochloric acid; the later part, the hydrolysis of certain of the simpler peptones which do not give the biuret reaction, under the influence of erepsin. The evidence that proteins are completely broken down to simpler amino acids during digestion and absorbed as such is now

generally accepted as fairly complete. It has been shown experimentally that a diet free from protein but containing instead either protein completely digested to its simpler amino acid constituents— or a mixture of amino acids artificially synthesized in the laboratory—suffices to maintain, and even to increase, weight for a considerable length of time; furthermore, the amino acids formed during digestion have been found in the blood and traced even into the tissues after absorption.

**Carbohydrates** in the intestine are split to simple monosaccharides. Under the influence of amylopsin, starch changes to maltose; the maltose is further split to glucose by the enzyme maltase secreted by the intestinal mucosa. Milk sugar is split to the monosaccharides glucose and galactose by the enzyme lactase. Cane sugar is split to glucose and levulose by invertase. Carbohydrates are absorbed as glucose, galactose, and levulose.

Under the action of the steapsin of the pancreatic juice **fats** are split into fatty acid and glycerin. The fatty acid combines with the alkali of the pancreatic secretion to form soap and is probably absorbed chiefly as soap. It has been generally taught that part of the fat may be absorbed unchanged in the form of a fine emulsion; this view probably still has adherents but is becoming less generally accepted. The splitting of the fat is not the only action to which fats are subjected in the intestine; the pancreatic juice, the bile, the alkali, and the churning movements of the intestine all aid in distributing the fat in the form of a fine emulsion which gives the greatest surface exposure and, therefore, the best opportunity for rapid action of the steapsin on the fat droplets.

The function of **bile** is very little understood. When, for any reason, bile does not pass into the intestine the feces become very foul and contain much fat. For this reason bile has been supposed to have an antiseptic action and to aid in the digestion and absorption of fats. Exactly how it aids the digestion of fats is not entirely clear; it probably accelerates the action of steapsin: the bile acids serve as a solvent for fats and fatty acid; and it is believed to aid in other ways in the emulsification of fats. Bile may limit putrefaction to a certain extent, but it is probably not a very efficient antiseptic; if fat is omitted from the food in cases in which bile is not reaching the intestines the stools are not foul. It appears, therefore, that it is the large quantity of fat and not the absence of bile alone which is responsible in these cases for the putrefaction. It may be that the undigested fat present in such large quantities coats over and protects the rest of the food from the action of digestive enzymes.

The absorption of the end products of digestion goes on chiefly in the small intestine—carbohydrate and protein end-products into the capillaries, fat into the lymphatics—but the mechanism of absorption is not entirely clear. Diffusion and osmosis can take place through the intestinal wall—this may account for the flow of water into the intestinal lumen under the influence of the hydragogue cathartics; but the laws of diffusion and osmosis, as we understand them at present, do not seem to explain entirely the normal absorption from the intestine. Whether or not a substance will be absorbed in the intestine depends partly on the chemical na-

ture of the substance and not altogether on the relative concentrations of the substance on the two sides of the intestinal wall. Sodium sulphate, for example, though there is none in the blood, may fail to be absorbed at all; the blood serum of an animal, on the other hand, in spite of the fact that the concentration of all the constituents of the serum is the same on both sides of the intestinal wall, may be completely absorbed if placed in the lumen of the intestine of the same animal. It is probable that the laws of diffusion, osmosis, adsorption, and chemical equilibrium are at work, but that their action is somewhat obscured by the fact that between the intestinal lumen and the blood stream lie layers of cells containing colloids; and that the nature of the colloid—being determined not only by its composition but by its content in salts, acids, bases, and water—may be different in that part of the cell adjacent to the intestinal lumen from what it is in that part adjacent to the blood stream—a difference, moreover, that can be constantly maintained by the diffusion of substances from the ever-moving blood stream—so that equilibrium between cell contents and intestinal contents may not be reached and certain substances may move constantly in one direction.

The **motor activity** of the intestine consists of several kinds of movements. One kind, the so-called pendulum movement, is a rapid churning which thoroughly mixes the food and facilitates digestion and absorption by bringing the material into intimate contact with the digestive juices and absorbing surfaces of the intestinal wall; the stream of food is broken up into small segments which re-

combine and break up again repeatedly; there is no steady progression of the stream. A second form of movement, the true peristaltic movement, consists in peristaltic contractions which move the food along the length of the intestine. A third form of movement, the so-called rolling movement, consists of infrequent but violent waves of contraction which pass over a large portion of the intestine at one time and which move the contents of the intestine rapidly along for a considerable distance at a time; such infrequent waves of contraction pass along the large intestine about half a dozen times a day and are preliminary to defecation. Other forms of movement are the antiperistaltic waves which push the intestinal contents away from the rectum and toward the stomach—a form of movement which is of therapeutic significance in rectal feeding—and the snake-like gyrations that twist the gut on its mesentery.

The function of the **large intestine** appears to be chiefly that of conserving the water of the tissues by inspissating the feces; several liters of fluid per day are secreted in the mouth, stomach, and intestines, and the contents of the intestine as they pass through the ileo-coecal valve are in the form of a thin fluid; by the time they reach the rectum they are semi-solid. Studies of animals from which the small intestine has been removed for experimental purposes show that a certain amount of digestion and absorption can take place in the large intestine; this capacity to digest and absorb is sometimes made use of therapeutically in rectal feeding. The subject has not been much studied but undoubtedly enzymes from the small intestine are carried into

the large intestine and possibly continue digestion there.

The fact that about one-third of the total weight of feces is made up of the bodies of bacteria is evidence that there is considerable **bacterial activity** in the gastro-intestinal tract. The possible significance of this bacterial activity has been much discussed and opinions vary between two extremes; certain investigators insist that bacteria perform necessary functions in the intestine without which an animal cannot live; others believe that bacterial activity is not necessary and may be very harmful and that it is the chief cause of the general decay and loss of vitality seen in old age. It is undoubtedly true that marked grades of intestinal putrefaction can give rise to symptoms and there is a general tendency to attribute certain obscure rheumatic, neurasthenic, and nutritional disturbances to the intestinal putrefaction with which they are sometimes associated; but definite proof is still wanting and there is no agreement among physicians on the question of how much disease is due to this cause. Normally, the bacteria act chiefly on the carbohydrates of the food and give rise to alcohols and the simpler fatty acids; these are not harmful; on the contrary, they serve to stimulate peristalsis; the acids neutralize the alkaline reaction of the secretions and so keep the contents of the intestine neutral or slightly acid—a reaction which is unfavorable for the action of putrefactive organisms on proteins. When taken in large quantities, however, easily fermented sugars like glucose may give rise to these products of fermentation in quantities sufficient to cause considerable gastro-intestinal irrita-

tion. In the case of the proteins the amino group may be split off from the amino acids giving ammonia; and various organic acids may be formed by oxidation and splitting off of carbonic acid. Thus

$$\text{Alanin}\quad \begin{array}{l} CH_3 \\ | \\ CHNH_2 \\ | \\ COOH \end{array} \quad \text{gives Propionic Acid} \quad \begin{array}{l} CH_3 \\ | \\ CH_2 \\ | \\ COOH \end{array}$$

$$\text{and}\quad \text{Acetic Acid}\quad \begin{array}{l} CH_3 \\ | \\ COOH \end{array}$$

A little more complex possibility is seen in the case of tyrosin; by a series of reactions the following products are formed:

$$\begin{array}{ccccc} \begin{array}{l} C_6H_5OH \\ | \\ CH_2 \\ | \\ CHNH_2 \\ | \\ COOH \end{array} & \rightarrow & \begin{array}{l} C_6H_5OH \\ | \\ CH_2 \\ | \\ CH_2 \\ | \\ COOH \end{array} & \rightarrow & \begin{array}{l} C_6H_5OH \\ | \\ CH_2 \\ | \\ COOH \end{array} \rightarrow \\ \text{Tyrosin} & & \begin{array}{c}\text{Para-Oxyphenyl-} \\ \text{propionic Acid}\end{array} & & \begin{array}{c}\text{Para-Oxy-} \\ \text{phenylacetic} \\ \text{Acid}\end{array} \end{array}$$

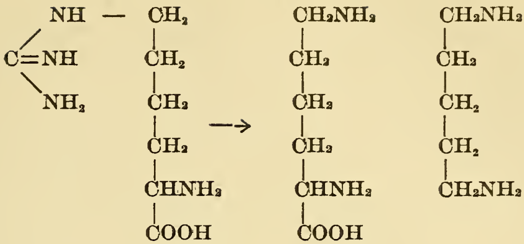
$$\begin{array}{ccccc} \begin{array}{l} C_6H_5OH \\ | \\ CHOH \\ | \\ COOH \end{array} & \rightarrow & \begin{array}{l} C_6H_5OH \\ | \\ CH_3 \end{array} & \rightarrow & C_6H_5OH \\ \begin{array}{c}\text{Para-Oxyphenyl-} \\ \text{glycollic Acid}\end{array} & & \text{Para-Kresol} & & \text{Phenol} \end{array}$$

The carboxyl group may be split off leaving an amine; thus from

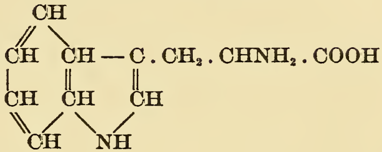
$$\text{Lysin}\quad \begin{array}{l} CH_2NH_2 \\ | \\ CH_2 \\ | \\ CH_2 \\ | \\ CHNH_2 \\ | \\ COOH \end{array} \quad \longrightarrow \quad \text{Cadaverin} \quad \begin{array}{l} CH_2NH_2 \\ | \\ CH_2 \\ | \\ CH_2 \\ | \\ CH_2NH_2 \end{array}$$

may be formed; and from

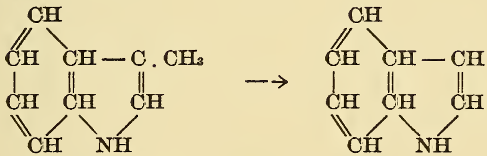
ARGININ ORNITHIN PUTRESCIN



TRYPTOPHAN



may give rise to



SKATOL AND INDOL

Many of these products are poisonous; small amounts of them are formed normally, absorbed, and excreted in the urine in combination with sulphuric acid; in large quantities they are believed by many physicians to be responsible for a variety of symptoms. Putrefaction of proteins in the intestine may take place when carbohydrate is constantly absent from the diet or when—as the result, for example, of intestinal obstruction—there is stasis and the intestinal contents have become alkaline. In the small intestine, where carbohydrate is available, the normal products of bacterial activity are chiefly the harmless fatty acids; in the large intes-

tine, where carbohydrates are not present to keep up an acid environment by their fermentation, putrefaction of the proteins goes on and the more poisonous products may be formed.

**Recapitulation.** To summarize briefly the fate of the different foodstuffs in the gastro-intestinal tract: Proteins are dissolved and undergo a slight preliminary splitting in the stomach under the influence of pepsin-hydrochloric acid. In the small intestine they undergo further splitting to relatively simple peptones and still simpler compounds under the influence of trypsin; and under the influence of erepsin they are completely split to simple amino acids in which form they are absorbed into the circulation and carried into the tissues. The splitting of starch to maltose begins in the mouth under the action of ptyalin. In the cardiac end of the stomach digestion continues under the influence of the same enzyme and more starch is set free from the cells as a result of solution of the intercellular material. Carbohydrate digestion is completed in the small intestine under the influence of amylopsin, the disaccharides being there split under the influence of maltase, lactase, and invertase to monosaccharides and are absorbed into the blood stream as monosaccharides. In the stomach, fat is set free from the connective tissue cells of the food as a result of the solution of these cells by pepsin-hydrochloric acid and it is melted and distributed in the form of a coarse emulsion. In the intestine it is still more finely emulsified, then split into fatty acid and glycerin; the fatty acid combines with alkali to form soap and the soap is absorbed through the lacteals into the lymph stream. Salts and water are absorbed in the intestine.

## Influencing the Digestive Functions.

The gastro-intestinal tract has secretory functions, motor functions, digestive functions proper, and absorptive functions; and all of these functions may be influenced—increased or diminished—by dietetic methods—the nature and quantity of the food—by drugs, and by many other means. Dietetic measures are especially important. Proteins, fats, and carbohydrates all have different effects in influencing digestive functions. Combinations of these foodstuffs may bring about other results. Any one of these three kinds of foodstuffs may come from the animal or from the vegetable world, with a resulting difference in the effect on the digestion. The different proteins, fats, and carbohydrates may vary much in their chemical composition and physical properties according to their source. Protein food may contain much tough connective tissue; it may be taken in large pieces, or in a finely divided condition. Moreover, the nature of the cooking process—boiling, frying, roasting—brings about a further alteration in the food. All these and other factors are important in determining what the effect of the food will be on the function of the gastro-intestinal tract.

**Influencing secretion.** The quality and quantity of the secretions may be influenced directly by substances present in the food or indirectly through the nervous system. Some foods contain substances which have been called secretagogues, substances that directly stimulate the flow of gastric juice when they are placed in the stomach; meat extracts and soups are especially rich in them. Bread, eggs,

and milk do not contain these substances, but the first products of digestion do; so that as soon as digestion starts, secretagogues are produced which serve to keep up a continuous flow of gastric juice so long as digestion continues. Secretagogues belong to the class of substances known as hormones—substances which act not through the nervous system but directly on the secreting cells. One of the best known of these is secretin; this is formed in the mucosa of the duodenum as the result of the action of the acid gastric contents of the stomach; it is carried by the blood stream to the pancreas and there stimulates the secretion of pancreatic juice.

The quality and quantity of the food determine not only the amount of secretion, but also its nature; there is a very accurate adaptation to the work required. Thus the gastric juice secreted after eating bread is less in quantity, but has a greater digestive power than that secreted after meat; the pancreatic secretion following protein foods is especially rich in trypsin, that following fat, rich in steapsin. It seems probable that secretion is caused not by general stimuli all affecting the cells alike, but by specific stimuli due to substances in the food whose action is such as to give rise to the secretion best adapted to the work required in each case.

The secretions may be affected through the **nervous system.** The sensations set up during mastication, acting through the nervous system, serve to stimulate gastric secretion. This takes place even when the food does not reach the stomach and can be demonstrated in dogs with oesophageal fistula; if such a dog is allowed to chew meat which later passes out through the fistula so that it does not

reach the stomach, digestion will be found to be far more rapid in the stomach of this dog than in the stomach of a control animal which has not had anything to chew. Even more subtle influences affect digestion. It is a common observation that the taste, smell, sight, and even the thought of food often serve to stimulate the flow of saliva. Everyone knows the effect of excitement and unpleasant emotions in repressing the appetite and digestion; and experimental observations on lower animals and on human beings have shown that sorrow, anger, and fear inhibit the gastric secretions. The company and other details of the environment often have a marked effect on the appetite and digestion. Persons who are well at home often suffer from digestive disorders when travelling and eating in hotels. Such psychic influences have been studied experimentally in animals and it has been demonstrated that indirect stimulation of secretion and digestion through psychic and nervous influences is very marked. Dilute acid, for example, stimulates the flow of saliva in the dog; if, now, dilute acid slightly colored with dyestuffs is given repeatedly for a considerable length of time, finally the psychic effect of simply showing the dog the colored fluid leads to the secretion of saliva. Secretions can also be influenced through the sense of hearing; if a certain set of tones is always played to a dog just before he is given meat—the meat stimulates the flow of saliva—finally secretion of saliva begins as soon as the tones are heard and before the meat is given. Strong emotions may completely inhibit the secretion of digestive fluids; it has been shown, for example, that gastric secretion is inhibited in a dog

when he is worked up into a rage by the presence nearby of a cat. These findings have been confirmed for man by experimental studies of persons with accidental fistula. The therapeutic importance of psychic influences on digestion is great and, in digestive disturbances, many details of the environment may serve to stimulate or to depress digestion.

The secretions can be influenced also by **drugs.** Although **alcoholic drinks** have long been used for their supposed beneficial effect on digestion, it is only in recent years that this action has been the subject of experimental study; the results have shown that in anything more than small quantities the action is deleterious. The action of alcohol in small quantities is somewhat complicated and not exactly clear; it causes an increase in the flow of saliva and gastric juice partly from a direct irritant action of the alcohol on the cells and partly from indirect action; the indirect action is seen in the increased flow of gastric juice following administration of alcohol per rectum and in the increased flow of gastric juice in a portion of the stomach isolated so that no alcohol reaches it following administration of alcohol per mouth. The increased secretion affects not only the fluid but also the acid and ferments of the gastric juice; there is, however, some evidence that the active pepsin itself is not always increased but only the propepsin. The effect on the rate of digestion is not entirely clear; digestion is sometimes accelerated, sometimes retarded; there is some evidence that so long as the alcohol remains in the stomach digestion is retarded but that afterwards digestion proceeds faster than if alcohol had not been given. If to this experimental data we

add the results of clinical experience, we can say that small quantities of alcoholic drinks taken just before or with the meals stimulate the appetite and, so far as the subjective symptoms, which are often the object of treatment in digestive disturbances, are concerned, digestion is improved.

Bitters—gentian, nux vomica, capsicum, quinine—and pungent substances are often used to improve the appetite. These substances are said to lead to an increased secretion of gastric juice—though this is denied by some investigators—not only as the result of direct stimulant action on the stomach but from indirect action; they stimulate the salivary glands and the effect may be produced simply by rinsing out the mouth with them. Nicotin also affects digestion; the satisfaction derived from an after-dinner cigar may, perhaps, be explained in part by the effect of small doses of this drug in stimulating glandular action; larger doses and chronic nicotin poisoning decrease the flow of gastric juice. Salt, spices, mustard, and pepper also stimulate the gastro-intestinal secretions. The stimulating action of pilocarpin, physostigmin, and other drugs of this group on glandular secretion are rarely made use of. Practically the only substances we know of which stimulate the secretion of bile—aside from sodium salicylate which has a slight cholagogue action—are bile itself and the bile acids.

Atropin and alkaline substances are sometimes used to inhibit hypersecretion in the stomach. Colloid substances, like gum-arabic and starch, and insoluble powders, such as bismuth subnitrate, are sometimes given with the hope of coating the stomach wall and protecting it from the stimuli that

provoke hypersecretion; bismuth salts, too, are said to increase the secretion of mucus, and this is believed to act as an added protection.

**Influencing motor activities.** The movements of the gastro-intestinal tract are in part automatic and myogenic, originating in the tract itself, and in part under nervous control; the rhythmic segmentations which simply churn and mix the contents of the intestine, without causing them to progress, are automatic; the peristaltic movements are under the control of the nervous system. The movements can be influenced by the nature and by the quantity of the food. Water and carbohydrates begin to pass out of the stomach almost as soon as they are introduced; proteins remain a somewhat longer time, and fats longest of all. When fats are mixed with other foodstuffs they delay the passage of the food from the stomach. If carbohydrates are given first and then proteins, the carbohydrates pass out of the stomach quickly, the protein only later; if carbohydrate is given after protein the passage of the carbohydrate out of the stomach is delayed by the protein. The contractions of the intestine are probably due in part to mechanical stimulation—local distention—by the food; food containing much coarse, indigestible material, such as cellulose, is believed to stimulate peristalsis. Contractions are also stimulated by the chemical irritation of certain of the substances formed in the fermentation of carbohydrate food—methane and lower fatty acids.

**Nervous and psychic influences** affect the gastro-intestinal movements; strong emotions, such as anxiety, distress, and rage can inhibit all movement; certain psychical conditions—excitement, fear—are

sometimes accompanied by greatly increased motor activity.

The motor activity of the tract is influenced by sudden changes in the blood supply, and by various **drugs.** Activity is increased by small doses of alcohol or nicotin, and by the cathartics. Nicotin probably stimulates the motor-nervous mechanism. The action of the hydragogue cathartics is probably accounted for in part by the mechanical stimulation of the large quantities of water attracted into the bowel; possibly, also, in the case of the sulphates, citrates, phosphates, and other calcium precipitating compounds, by the decrease in the calcium content of the intestinal musculature whereby rhythmic contractions are set up. The other cathartics probably owe their activity to direct irritant action on the muscles and nerves of the bowel. Castor oil acts chiefly on the small intestine; it is absorbed before reaching the large intestine. Certain of the other cathartics, especially senna, aloes, rhubarb and cascara, act on the large intestine; they cause reflex irritation and congestion of other pelvic organs, especially the uterus, and should not, therefore, be used in menstruating or pregnant women.

Motor activity is decreased by morphine and by atropin. Morphine decreases the motor activity of the intestine and the frequency of evacuation and leads to the excretion of less watery stools. This is due to the direct effect on the bowel itself and not to action through the nervous system; the crude preparation opium is, therefore, on account of its slow absorption and prolonged local action, better in this case than the pure alkaloid. Atropin has, on the whole, a sedative effect on the gastro-intesti-

nal tract. Its action is somewhat difficult to explain; the results of investigation indicate that, by stimulation of the myenteric plexus (Auerbach's) it excites motor activity while at the same time relaxing and quieting the nerve endings of the vagus through which motor impulses reach the intestine, especially when these are unduly excited. These apparently somewhat contradictory actions are, however, in harmony with the fact that while atropin does relieve convulsive contraction of the intestines, such, for example, as that resulting from lead poisoning, it not only does not overcome the action of cathartics, but actually favors their action and overcomes the griping produced by the more violent ones.

**Influencing Absorption.** We know very little about methods of affecting the rate of absorption of food. The most easily digested foods are, of course, most readily absorbed; vegetable proteins and fats, for example, are less readily absorbed than animal proteins probably because they are enclosed in cells with more difficultly digestible membranes. The melting-point of fats also affects their absorption; very solid fat may be poorly absorbed. White of egg, or glucose, when given in large quantity, may be absorbed so readily as to be excreted in the urine before they can be utilized by the body. Small amounts of alcoholic drinks improve absorption. The beneficial effect of arsenic treatment in undernourished persons is ascribed by some to improvement in absorption, resulting from dilatation of the capillaries and small vessels of the splanchnic area. It is believed also that certain pungent irritating substances, like pepper and mustard, increase the

power of absorption. Mucilaginous and colloid substances, like starch and gums, retard absorption; when we want to retard absorption so as to get a prolonged local effect on the gastro-intestinal tract rather than a constitutional effect, this fact is made use of in giving colloid-containing crude drugs, like nux vomica or opium, rather than strychnine or morphine. Absorption is decreased, too, by accelerating the passage of foodstuffs through the intestine with purgatives.

**Interrelation of functions.** There is an intimate relationship between the functions in the different parts of the gastro-intestinal tract; mention has already been made, for example, of the effect of mastication of food on the function of the stomach and of the influence of the digestive changes in the stomach on intestinal digestion. It is clear, therefore, why disturbances in one part may affect functions in a lower part of the tract. If, for example, hydrochloric acid secretion in the stomach is greatly diminished, evacuation of the stomach will be more rapid as a result of the more speedy neutralization of the acid—the presence of which keeps the pylorus closed—in the duodenum; the absence of normal stimuli for secretin formation may lead to retardation of protein digestion through diminution of the secretion of pancreatic juice—a retardation which may be still further increased by the failure of the normal preliminary preparation of the protein food in the stomach; fats may be insufficiently digested as a result of failure of the stomach juices to dissolve the connective tissue cells; on account of incomplete solution of pectin and vegetable proteins starch may not be set free from the cells in

which it is contained; and harmful putrefactive bacteria may pass alive through the stomach and into the intestine. This matter of interrelationship of the various gastro-intestinal activities is probably far more highly developed and important than we realize at present.

## Pathological Part.

A knowledge of the rational methods of treating diseases of the gastro-intestinal tract depends upon an understanding of the methods of increasing and decreasing the various functions of this tract; the treatment consists chiefly in an application of the methods already outlined for increasing and decreasing function. Treatment may be required for the functions as a whole or for the nervous mechanism, the motor mechanism, or the secretory mechanism alone. The functions as a whole are given rest by withdrawal of all food, and by complete bodily rest in bed, and are stimulated by large quantities of food. Rest is given in all acute conditions—gastritis, gastro-enteritis, hemorrhage, ulcer—or when, for any reason, there is danger of perforation. If the condition is of brief duration, as in an attack of acute gastritis, all food and drink, even water, may be withheld and the patient starved for a short time; if the condition is of longer duration and localized, say, in the stomach, food may be administered per rectum. A complete discussion of all the possible ways of treating the many diseases of the gastro-intestinal tract would fill volumes; the brief discussion which follows is intended not at all as a detailed list of methods, but merely as an

illustration in outline of the application of these principles to a few of the more common diseases.

**Acute Gastritis.** In mild cases of acute gastritis following an indiscretion in diet often no treatment is necessary; the patient usually quickly recovers without special treatment. In more severe forms all food should be omitted for a day or two. The removal of material responsible for the condition should be facilitated by emetics—warm water is the simplest; and cathartics—castor oil and calomel are the best in these conditions.

**Ulcer and hemorrhage.** In cases of ulcer or hemorrhage, rest for weeks may be necessary; the patient should be kept in bed as quiet and free from excitement as possible. Nourishment can usually not be entirely withheld for any length of time; small amounts of bland liquid or semi-liquid food, such as beef tea, egg albumin, and even milk may be borne. In cases of gastric ulcer sometimes even the smallest amounts of food cause irritation and it may be necessary to resort to rectal feeding; when even this causes irritation, we may have to starve the patient for a short time. Some physicians, indeed, rarely, if ever, resort to rectal feeding. The absorptive power of the rectum and large intestine for foodstuffs is not ordinarily called into play; nevertheless a few ounces of peptone and a similar amount of carbohydrate per day can be absorbed when given per rectum. An enema consisting of one egg beaten up in 200 grams of milk to which one-quarter to one-half teaspoonful of salt has been added—the salt aids absorption—may be given every six hours; if the rectum is sensitive, 8 or 10 drops of tincture of opium may be added.

Pillows should be placed under the hips and the enema introduced high up so that the irritation will not lead to expulsion. Antiperistalsis may carry enemata a variable distance backward along the gastro-intestinal tract; it has been stated that material given per rectum may reach even the stomach. Nutrient enemata may cause pain and secretion of acid in the stomach so that in severe cases food should be administered in this way only in moderation. Belladonna may be given to decrease the secretion of acid in the stomach and alkalies to neutralize excess of acid. Bismuth subnitrate and other bismuth compounds are given to coat over and protect the surface of the ulcer and to increase the formation of mucus which also protects. To quiet the gastro-intestinal tract when there is hemorrhage and vomiting an ice bag may be placed on the abdomen, and opium or atropin administered. Under certain conditions—in cases with severe and repeated hemorrhage, in frequently recurring, intractable cases, or in cases where perforation has taken place—the surgeon may be called on to operate.

With improvement in the condition, the patient need rest in bed only a short time after meals; this facilitates the emptying of the stomach. When food is again given per mouth only small amounts should be given at first and this should be in the form of liquids and semi-solids—white of egg, strained gruels, thin soups. Later, soft toasts and chopped meats, but not vegetables, may be given; the small amounts may be given at frequent intervals. As the amount of food given per mouth is increased, the amount per rectum should be decreased. In

cases of gastric hemorrhage or ulcer, the treatment may have to be continued for a long time, and coarse foods, such as bread crusts, the skin and seeds of fruits and woody vegetables, alcoholic drinks, and sharp condiments, should be avoided. Certain very exact diets for the different stages of gastric ulcer named after the proposers are to be found in the literature; these are useful as examples of how the principles of treatment may be applied, but it is better to prescribe a diet adapted to the individual patient in each case and not adhere to any rigid formulas.

The treatment outlined for ulcer applies to ulcer of the stomach and of the small intestine. In cases of ulcer of the large intestine, the nutrient enemata are, of course, not given, but the other dietetic measures are the same as for ulcer of the small intestine; the bulk of the food should be kept low, and coarse vegetables and fruits, which give bulky, irritating feces, should be excluded; in order to give the ulcer a chance to heal during sleep, cleansing enemata may be administered at night. Powdered chalk, quinine, and iodoform per rectum are also administered. Quinine is given at first in dilution of 1 to 5000 and then in increasing strength up to 1 to 2000; it should be removed after each treatment. Iodoform may be given in the form of an emulsion with mucilage and water; it should be removed after fifteen minutes. Silver preparations—generally given with morphine on account of the pain they cause—followed by normal salt solution to wash out the excess of the silver compound, are sometimes applied to the ulcers. Surgical intervention is often necessary to remove the ulcer or, in

the case of chronic tuberculous ulcer, to short circuit the feces through an artificial anus so that the ulcerated lower bowel may have a long period of rest.

**Disturbance of the nervous, motor, and secretory mechanism.** In disturbances of the nervous, motor, or secretory mechanism every effort should be made to find the cause of the trouble so that intelligent treatment may be given to relieve it. On account of the close interrelationship between the different gastro-intestinal functions, a disturbance of one function may be merely a consequence of a disturbance of some other function; or some underlying disorder may be responsible for disturbances of various functions. The source of the trouble may be in the gastro-intestinal tract itself, or in the nervous mechanism controlling the tract; it may be the result of disease in some other organ, or the result of constitutional disease—heart disease. nephritis, arteriosclerosis, or disease of almost any organ in the body. It is often, however, impossible to find any anatomical basis for most distressing and far-reaching symptoms; the therapy of such cases brings out the value of treatment directed at function, without reference to the anatomical basis. The amount of food may be too great; too much food and a sedentary life are incompatible; relief from gastro-intestinal disturbances frequently follows changing to a diet of low caloric value. The trouble may be due to improper food; too much greasy food may cause indigestion; too much carbohydrate food in the form of sugar can lead to excessive fermentation in the intestine; under certain circumstances too much meat may be harmful.

Many persons show special intolerance to certain articles of diet. Sometimes it is the preparation of the food that is at fault; the food may be good but improperly cooked. The food may be swallowed before it is sufficiently chewed, or the meals may be eaten in a condition of excitement or anxiety or at improper times, such as before going to bed or just before certain kinds of severe labor. Even more subtle—psychic—influences surrounding the serving and eating of food may be responsible for indigestion. In order that all undesirable factors may be eliminated, detailed inquiries regarding the dietetic habits of the patient should always be made. It is impossible to lay down rigid rules for treatment; considerable experimentation may be necessary before a successful form of treatment is found.

**Motor Mechanism: Constipation.** The commonest form of gastro-intestinal disturbance that the physician has to treat is constipation. There is some disagreement among physicians as to the necessity of a movement of the bowels every day. Many persons remain in apparently good health in spite of infrequent movements; but in persons with constitutional disease such as nephritis or arteriosclerosis, or when constipation is followed by headache, lassitude, loss of appetite, furred tongue, or bad taste in the mouth, efforts should be made to bring about one good movement a day. If some definite cause can be found for the constipation—atony, spasm, weakness of the abdominal muscles, obesity, stricture, adhesions—attempts may be made to treat these; but in the greater number of cases there is no such definite cause; the condition is due to improper diet, sedentary habits, constitutional peculi-

arities, or some other unknown cause. In such cases, it is better, if possible, to avoid drugs; the patient becomes dependent on the drugs and, later on, furthermore, the body tolerates the drug without responding and some other drug must be used.

**Dietetic measures** are usually more satisfactory. Fruits and vegetables containing much cellulose, bread made from whole wheat flour, and coarse oatmeal stimulate the intestine. Honey, molasses, marmalade, jellies, and other foods rich in sugar are mildly laxative; the sugar retards absorption of water in the intestine and is fermented in part, besides, to stimulating fatty acids. Milk sugar is also laxative. Prunes, figs, plums, dates, peaches, cherries, and berries have a mildly aperient effect—due to their content of sugar, fruit acids, and salts. Often the patient does not drink enough water; cold water taken on an empty stomach is often effective. The bland food oils, such as olive oil and cottonseed oil, not usually considered cathartics, often seem to have a mild stimulating effect on the intestines.

Nicotin stimulates peristalsis; a cigar or a pipeful of tobacco after breakfast sometimes acts very efficiently. Movements of the bowels are sometimes facilitated by having the patient take the knee-chest position and constipation can sometimes be overcome in this way. Massage of the abdomen sometimes helps; the same principle is utilized when a heavy ball weighing four or five pounds is rolled over the abdomen for five or ten minutes every morning.

If more active treatment is necessary, **cathartics** or enemata may be used. There is a long list of cathartics varying in activity from the very mild

saline laxatives to the drastic vegetable purgatives; if one does not act, another may. The very mild saline cathartics, such as the sulphates, phosphates, and citrates of sodium, potassium, and magnesium, and the milder vegetable cathartics, such as castor oil, cascara, aloes, compound liquorice powder, and rhubarb, are used most frequently. The saline cathartics act by attracting water into the intestines and are, therefore, especially valuable in diseases of the heart and kidneys accompanied by edema and dropsy. Except compound jalap powder, the powerful drastics—members of the jalap and colocynth groups—are not much used except for maniacal or unconscious patients. On account of their effect in causing congestion of the pelvic organs, senna, aloes, rhubarb, and cascara should not be given in cases of pregnancy or piles; a mixture of sulphur, cream of tartar, and molasses can be given instead.

**Enemata** in the form of plain tepid water, or, better, tepid soapsuds may be used. A glycerin suppository, or injection of a small amount of glycerin, may be tried. A tumblerful of olive oil, cottonseed oil, or Russian mineral oil, introduced slowly about five or six inches into the rectum, is effective; pillows should be placed under the hips so that the oil will be retained. The oil enema should be given every day for about ten days, then every other day, later every third day, and then, finally, omitted.

Atropin is sometimes useful in relieving constipation due to convulsive contraction of the intestine.

**Atony of the stomach.** Inactivity—atony—of the stomach may result in dilatation as a consequence of the accumulation of the large quantities of material,

and the stagnant material may then undergo fermentation; water may be secreted into the stomach and the patient may vomit a larger volume than he eats. This condition is often present in persons who are run down, undernourished, nervous, and overworked, and attention should, therefore, be directed to the general health as well as to the gastric disturbance. Bulky foods, such as fruits and vegetables, and easily fermentable substances, such as sugar, should be diminished, and only concentrated foods given. The food should be taken in several small meals rather than three larger ones. The amount of fluids taken should be limited. Strychnine may be of value in stimulating gastric activity. If there is any lack of hydrochloric acid in the stomach, this deficiency should be corrected. If food remains in the stomach half a day, or, after a heavy meal at night some of the meal is still found in the stomach following a test breakfast next morning, the stagnant food may be washed out with a stomach tube; the patient himself can be taught to do this; there are wide differences of opinion among physicians on the question of the desirability of instituting such a régime.

**Diarrhea.** Diarrhea may be the result of infectious or of constitutional disease—dysentery, cholera, tuberculosis, cancer, anemia, malnutrition, disease of the heart, lungs, liver, kidneys or nervous system—or the result of changes in the weather, a chill, or an indiscretion in diet. The question of diagnosis is important because the form of treatment differs somewhat according to the cause.

In cases of **acute diarrhea** following a chill, or the result of infected food, or other indiscretion of diet,

direct attempts to stop the diarrhea should not be made; evacuation of the bowels should be facilitated and, by the use of calomel and castor oil, all efforts made to expel the putrefying or bad food. Large doses of bismuth subnitrate or chalk may be given to protect the mucous membranes of the intestines; and charcoal, and colloidal and viscous substances to absorb the poisonous material as well as to protect the intestinal wall and prevent absorption by the body.

In cases of **chronic diarrhea** the infectious or constitutional disease responsible for the condition should be treated. The diarrhea may also be treated more directly by dietetic measures; all irritating, stimulating foodstuffs, such as coarse vegetables and fruit containing much cellulose, should be decreased or omitted; carbohydrates are usually digested better than fats. Sometimes tea, blackberry brandy, or other drinks containing tannin are helpful. A strict diet of nothing but boiled milk may be found necessary in some cases. Certain articles of food cause diarrhea in some persons; such articles of food should be forbidden them. Small doses of salol, thymol, or carbolic acid are sometimes given to combat the intestinal putrefaction responsible for the diarrhea; but although these can serve to disinfect the duodenum, it has been shown that no medication can influence the flora of the rest of the small intestine; this can only be regulated by diet and evacuations. Intestinal putrefaction and diarrhea are sometimes due to the absence of sufficient carbohydrate in the diet; a certain amount of carbohydrate normally undergoes fermentation giving rise to organic acids which inhibit the putrefaction of

proteins. Putrefaction may be due to the lack of hydrochloric acid in the stomach; the acid gastric juice is believed to kill those bacteria responsible for putrefaction of proteins, and when this acid is absent the putrefactive organisms may reach the intestine. Complete rest in bed, especially after meals, is advisable in cases of chronic diarrhea. Large doses of bismuth subnitrate are useful. In cases of diarrhea due to increased nervous irritability, opiates and bromides are useful. Sometimes an entire change of air and surroundings gives the best results. When diarrhea is due to ulceration of the large intestine, the methods already outlined for treatment of ulcer should be used.

**Secretions: Hyperacidity.** A differentiation between hyperacidity and hypoacidity, although easily made after examination of the stomach contents, is not always easily made on the symptoms. Without resort to washing out the stomach contents, a diagnosis can, nevertheless, sometimes be made simply by trying the effect of alkali or acid treatment: if the symptoms become worse after acid, but improve after alkali therapy, it is probably hyperacidity; if the reverse is true it is probably hypoacidity. An increase in the acidity of the stomach contents may be due either to organic acids formed as a result of fermentation in the stomach or to excessive excretion of hydrochloric acid. A differentiation of these two conditions, easily made by examination of the stomach contents, is important since the treatment for the two conditions is not the same. Hyperacidity due to fermentation as a result of dilatation of the stomach and stasis of the food is treated by the methods already outlined;

administration of alkali, while neutralizing the acid present, would be followed by the formation of more acid.

The causes of hypersecretion of hydrochloric acid are unknown. Dietetic errors may sometimes be in part responsible—habitual overeating, especially of bread and meat, over-indulgence in fruits or foodstuffs, like fat-rich foods, for example, which delay gastric digestion. The gastric contents pass into the duodenum little by little, only as fast as the acid is neutralized; an increase in the acid concentration, therefore, retards the rate of evacuation, and the continued secretion of more acid leads to a still greater increase in the acid concentration: in this way a vicious circle is easily formed. Different individuals show widely varying degrees of tolerance to hyperacidity; marked hyperacidity, revealed only by analysis and not resulting in any apparent symptoms, is not uncommon and need cause no alarm.

The treatment of hyperacidity is chiefly dietetic. In order to decrease the excretion of excessive quantities of acid, only foodstuffs which stimulate the formation of acid as little as possible should be given; in order to use up the acid and keep its concentration as low as possible, foodstuffs with high acid combining power should be given. Milk is the foodstuff that most nearly fulfills these requirements and eggs hold second place. Meats and fish have a high acid-combining power. Unfortunately, meat and fish also stimulate acid secretion, not, however, so much on account of their protein content as on account of the extractives; since these secretagogues can largely be removed by boiling, boiled meat and fish have a place in the therapy of hyperacidity.

Bread is especially bad as a rule; it stimulates acid secretion, and has a low acid-combining power. Vegetable foods with much insoluble intercellular material, tough meat with much interstitial tissue, meat containing much fat, and meat that is not finely divided—all remain unduly long in the stomach before the gastric juice penetrates and dissolves them and are, therefore, unsuitable. Meat ought to be lean, tender, scraped, or finely chopped, and should be boiled to remove the extractives. Vegetables ought to be given with caution; they should be well cooked to dissolve the intercellular pectin as much as possible, and finely mashed. The question of carbohydrate food is a difficult one; since carbohydrates leave the stomach quickly and do not greatly stimulate acid secretion they would seem to be ideal foodstuffs; but the cells in which the carbohydrate is enclosed are often difficult of digestion, and clinical experience shows carbohydrate food to be often particularly bad. Condiments, such as pepper and mustard; tonics, alcoholic drinks, tobacco; coarse vegetables, and fruits; smoked, pickled, and highly salted food—all stimulate the secretion of hydrochloric acid and should, therefore, be used, if at all, only in moderation. Alkalies stimulate the excretion of acid and do not, therefore, constitute a part of the rational therapy, but may, nevertheless, be given at the height of digestion to relieve the sharp burning eructations. Atropin or belladonna is sometimes administered to decrease the secretion of acid. In every case the diet should be adapted to the individual patient; patients show many dietetic idiosyncrasies, and what may be good in the case of one patient may be harmful in another.

Sometimes one foodstuff—onions, beans, fat salt pork, and bacon, especially—may lead to hypersecretion. As pointed out in the opening paragraph of this section on gastro-intestinal diseases, a detailed discussion of treatment—and this refers especially to the details of dietetic treatment—would take us too far; but the considerations outlined in this paragraph on the treatment of hypersecretion give a general idea of the principles which determine how rational dictetic treatment is carried out.

**Hypoacidity.** Connective tissue is not easily attacked by the intestinal juices without previous gastric digestion, so that when hydrochloric acid secretion is deficient the meat in the food should be tender—with little fibrous tissue—and finely minced. Protein should be decreased and carbohydrates given instead. Salt, condiments, bitters—nux vomica, gentian, capsicum—alcoholic drinks, salted, smoked, and pickled meats may be given in moderation to stimulate secretion. Dilute hydrochloric acid itself may be given. In order to avoid the danger of atony and fermentation, the food should be taken in several small meals rather than in a few large meals. The condition occurs commonly in persons whose general physical condition is below par. Attention should, therefore, be given to the general hygiene of the patient; exercise, fresh air, hydrotherapy, climate and the effect of the environment on the mental and nervous condition should all be taken into consideration in the treatment.

**Intestinal worms.** Several remedies—known as anthelmintics—are used for **tapeworms** (taenia solium and taenia saginata); male fern (Felix mas),

pumpkin seeds, pomegranate seed, and cusco are among the best. Male fern, in the form of oleoresina aspidii, is one of the most used. Mixtures of different anthelmintics are said to be sometimes more effective than simple preparations. The best time to give the treatment is when parts of the worm are passed in the stools without treatment. For several days before the drug is administered the bowels should be well purged, the saline cathartics especially being used; the diet should consist of substances like fish, meat, eggs, and cereals like rice, which leave as little residue as possible; milk and coarse vegetables, which leave a large residue, should be omitted from the diet. The night before the drug is administered the patient is given onions, spices, pepper, or curry freely with the food—these are believed to favor the action of the drug. The next morning the drug is given followed by some black coffee. Several hours later a purgative is administered, preferably one of the saline cathartics or calomel; oils dissolve and favor the absorption of the active principle of the worm and should, therefore, not be given. If the head of the worm is expelled the treatment has been successful; if the head is not expelled the treatment should be repeated when parts of the worm again appear in the stool without treatment.

The commonest intestinal **round worm** (nematodes) are ascaria lumbricoides, oxyuris vermicularis, and uncinaria duodenalis. For **ascaris** the commonest remedy is santonin; this is given for several days in doses of two or three grains and is followed by a saline purge. Spigelia and chenopodium are sometimes used. **Oxyuris**, the pin worm,

affects chiefly children. Enemata of cold salt water —rather more concentrated than normal salt solution—combined with mild purgatives, are good; small doses of santonin may also be given. Sometimes more vigorous treatment is necessary; rectal injections of large amounts of fluid containing turpentine, vinegar, and even carbolic acid are used. For the itching, belladonna ointment may be applied. **Uncinariasis** is treated with large doses (2 grams) of thymol. Two doses are given at two-hour intervals in the morning and these are followed two hours later by a cathartic. The day before and the day after the treatment the patient is given a milk diet.

**Symptomatic treatment.** The subjective symptoms associated with gastro-intestinal diseases are best attacked by treating the conditions responsible for them; practically the only symptoms which have to be treated independently as well are nausea, pain, and loss of appetite. When **nausea** is not caused by the presence of a large quantity of fermenting material in the stomach or by the absence of hydrochloric acid it can sometimes be relieved by swallowing small bits of ice or cold effervescing drinks; these slightly narcotize the mucous membrane of the stomach. **Pain** may be relieved by poultices and other hot local applications and counter irritants or by administration of narcotics such as morphine; when due to convulsive contractions of the intestine it can sometimes be relieved by atropin. The treatment of **loss of appetite** is often very difficult and all kinds of methods have to be tried. It is best to attack the symptoms from the psychic side; the food should be attractive in character, well cooked,

and served in an appetizing fashion. The treatment often requires rather a thorough understanding of the patient and his environment than special medical knowledge. Bitters—gentian, strychnine, capsicum—and alcoholic drinks are often helpful. In some cases, it may be necessary to resort to forced feeding through a stomach tube.

# DISEASES OF THE GENERAL METABOLISM.

There are pathological conditions which we do not think of as diseases of any individual organ, but rather as disturbances of nutrition—disorders of the general metabolism—not that they may not eventually be shown to be primarily diseases of certain definite organs but because, at present, we do not know the organs responsible, and for the purposes of practical therapeutics they are, therefore, better treated as diseases of the nutrition of the cells as a whole. Among the disturbances of this kind are obesity, malnutrition, diabetes, and gout. For the treatment of these diseases a knowledge of the physiology of the general metabolism is indispensable; rigid rules for treatment cannot be laid down; therapeutics is simply a practical application of chemical and physiological knowledge. Such knowledge deals with the functions of various foodstuffs rather than the functions of organs and is applied in the treatment not only of diseases of metabolism proper, but in the treatment of many other conditions—fevers, heart disease, kidney disease, arteriosclerosis—as well. A brief outline of the important facts of metabolism is indispensable as an introduction to the treatment of metabolic disorders.

## Physiological Part.

The body has been compared to a steam engine: both take in material having a high potential ener-

gy, oxidize this material, and set free the energy; in both cases the energy appears partly in the form of heat, and partly in the form of work. But, unlike the steam engine, the body utilizes part of its fuel material to renew its own structure. Furthermore, the three principal foodstuffs, though in part interchangeable, are not entirely so; each has its own function.

On account of the similarity in chemical composition between protein food and muscle, the early physiologists believed protein food to be the sole source of energy for muscular contraction; carbohydrates and fats were believed to be utilized only as a source of heat production. When it was demonstrated that practically all the end products of nitrogenous metabolism are excreted through the kidneys, and that, therefore, a determination of the amount of nitrogen in the urine serves as a measure of the amount of protein metabolized, an opportunity was given to investigate this hypothesis experimentally. Daily determinations of the nitrogen excretion made before, during, and after a day of severe muscular exercise—namely, mountain climbing—showed that, provided sufficient fat and carbohydrates are taken, there is no considerable increase in nitrogen excretion—and, therefore, of protein decomposition—as a result of muscular activity. Furthermore, on calculating even the minimal amount of energy that must have been used in raising the body from sea level to the mountain top, this was found to be greater than could be accounted for by the total amount of protein decomposed during the day. It became clear from these investigations that protein is not the sole source of

muscular energy. These findings led to new hypotheses regarding the nature of protein metabolism.

The hypotheses concerning the general nature of protein metabolism which have chiefly interested physiologists during the greater part of the last fifty years are those of Pflüger and Voit. According to Pflüger, protein food is first of all built up into living tissue before it undergoes oxidation. This hypothesis can hardly be correct; for when a large amount of protein food is taken at any one meal the nitrogen corresponding to this portion is all excreted within a few hours, and it is difficult to believe that it has all been built up into living protoplasm only to be at once broken down again. On this fact was based Voit's hypothesis according to which the nitrogenous food products pass through the blood into the different tissues and there become in great part catabolized under the influence of the living protoplasm, just like carbohydrate and fat, without becoming an integral part of the living protoplasm, only a small part being built up into living tissue to replace that lost by wear and tear. According to this conception, there are two kinds of protein in the body—living protein and circulating, dead protein—and the chemical processes constituting catabolism take place only in the circulating protein.

Until very recently we did not have sufficient experimental data to enable us to pass judgment on these two hypotheses. Such data are now available. Examination of the urine on diets of greatly varying protein content lends support to the view that we can divide protein metabolism into two parts—the metabolism of the living tissue, and the

metabolism of the food protein; for, among the nitrogen- and sulphur-containing end products of protein metabolism, we find two kinds of compounds, certain compounds like urea, the amount of which varies directly with the amount of protein in the food, and still others like creatinine, the amount of which does not depend at all upon the quantity of protein in the food, but on the body weight of the individual. Substances like urea which vary with the amount of protein food, are a measure of the metabolism of the food—the exogenous metabolism; substances like creatinine, which do not vary with the amount of food taken but depend on the body weight, are a measure of the metabolism of the tissues themselves—the endogenous metabolism.

Our present conceptions of the finer details of protein metabolism are based on recently acquired knowledge of the pure chemistry of proteins. All proteins are believed to be built up of complex combinations of about twenty different amino-acids. We believe that the food protein is broken up during intestinal digestion into these amino-acids and that these are then absorbed and carried by the blood to all parts of the body. Experimental evidence has not carried us much beyond this but possibly the tissue cells select what amino-acids they need to replace wear and tear, and the excess of amino-acids is then oxidized and utilized for energy, the nitrogen being split off as ammonia, the rest of the molecule having a history similar to that of the other nitrogen-free foodstuffs. It is this splitting off as ammonia that explains the greatly increased excretion of nitrogenous compounds in the urine after a diet rich in protein food.

Among the first practical questions that arise are those concerning the amounts of the different foodstuffs necessary or advisable in health and disease. It might be thought that, so far as protein food is concerned, determinations of the amount of nitrogen in the urine of starving persons would show how much nitrogenous food is necessary. But this is not so. The amount of nitrogen in the urine of a starving person depends on several factors—the length of time he has been starved, his previous diet and nutritive condition, and, when it is not a case of complete starvation, but only of starvation from protein food, on the character and quantity of the non-nitrogenous foodstuffs administered. Furthermore, if protein food containing just as much nitrogen as the starving individual excretes in his urine is administered, the metabolism will be raised to a higher plane and there will still be a negative nitrogen balance—a loss of nitrogen from the body. When the subject is studied still further, increasing complications are found and it turns out that a balance between intake and output of food can be brought about on different levels; we can have metabolism on a high plane or on a low plane. The question then becomes, which plane of equilibrium is best. This is very difficult to decide even in normal cases. It was assumed by physiologists, that people who could choose freely would instinctively take the amount and kind of food best suited to their needs and that, therefore, examination of the dietary of a large number of persons of different races, ages, and habits of life would show the quality and quantity of food best suited under different conditions. Variations were found. As was to be ex-

pected, persons living in a cold climate or engaged in active muscular work were found to consume larger quantities of energy-producing food. But, taking everything into consideration, there was a remarkable agreement in the dietaries of individuals living under similar conditions in different parts of the world. Tables prepared by different authorities showing the kind and amounts of food suitable under different conditions vary somewhat, but in round numbers 120 grams of protein, 500 grams of carbohydrate, and 50 grams of fat—equivalent in all to about 3000 calories—may be taken as average figures.

It is to be observed that these tables are based, not on any *a priori* reasoning as to the most suitable diets, but simply on the amounts found by examination of diets taken by instinct. It has been pointed out recently by many writers: first, that instinct may not lead us to take the most suitable diets; and, second, that, as a matter of fact, many individuals, without any observable ill effect, live on a much lower diet than that prescribed by the physiologists. Careful scientific investigation has confirmed the fact that an individual can live and work for a long period, without any apparent bad effect, on a diet very much poorer in protein and energy than that ordinarily chosen by the average individual; and some investigators believe that the average diet which man takes is not the amount necessary or even best for him. Certain investigators go even so far as to say that a very low diet is much better; that more work can be done; that various minor disturbances such as "rheumatic" pains, sick headache, and "bilious" attacks disappear; that there is

less tendency to mental depression; and that the intellect is keener. It is undoubtedly true of many persons who have reached middle life, that, in continuing to take the amount of food—and especially the amount of meat and other protein food—to which they have been accustomed in earlier life, they are taking more than is best for them; and clinical experience frequently demonstrates distinct improvement in the general condition on a more restricted diet.

There is, however, another side to this question: it is possible that the body can go for long periods on a low diet; but that under certain conditions the excess of foodstuffs not ordinarily needed may be necessary; and that, for this reason, nature has led us to use a high protein diet so that the cells may be constantly bathed in an excess of nutritive elements which can be used in times of stress. To make a comparison: it would be absurd to state that one person with no capital, who receives a daily wage that just pays his expenses, is as well off as another person receiving the same wage but having a reserve fund in the bank. Thoughout a period of many years, possibly, even, throughout life, it may never be necessary to draw on the reserve; but the occasion may suddenly arise at any moment when the reserve becomes a matter of life or death. Using teleology as a basis of justification is dangerously pseudo-scientific; but, in the absence of any other guide, we are on tolerably safe biological ground in believing that the sensations—excepting individual cases altered by disease—are intended for our protection and guidance: in the specific case of the amount and kind of foodstuffs needed under

various conditions, we have many examples—which would carry us too far to discuss—of how unerring is instinct. And so, until we have good grounds for abandoning them, we must have a proper regard for the high protein dietaries which are based on examination of the food intake of large groups of widely separated peoples. The excess of foodstuffs may be a nutritive factor of safety corresponding to the anatomical factor of safety provided by the possession of two lungs, two kidneys, and other organs either duplicated or enormously larger than is ordinarily necessary for carrying on the body work. Opinion, however, is still divided on this point.

All proteins are not equally valuable as foodstuffs. Some of them do not contain all the different amino acids necessary for nutrition. Gelatin, for example, does not contain tryptophan, tyrosin, or cystin, and an animal fed on gelatin only will lose flesh and finally die. Many of the vegetable proteins are deficient. It is not absolutely essential that all the different protein amino acids be present in a food protein. There is some evidence that the body has the power of synthesizing certain of them from other material —this seems true for glycocoll at any rate; certain other amino acids, tryptophan, for example, appear to be absolutely essential. The question of whether or not a diet containing even all the amino acids found in proteins is complete so far as nitrogenous constituents is concerned, is not yet entirely settled. Feeding experiments on dogs and rats had appeared to demonstrate so conclusively that maintenance and even growth are possible on a diet whose nitrogenous portion consists only of known amounts of the

amino acids of protein, that the belief had become generally accepted that these make up the only necessary nitrogenous constituents of the food. Recent investigations appear, however, to demonstrate that certain diseases, such as beri-beri and the polyneuritis of fowls, are due to a too restricted diet from which certain unknown constituents are missing; and studies of the relation of nutrition to growth, over long periods, indicate that unknown compounds are even more necessary for growth than for simple maintenance without growth. The importance of lipoids—lecithin, cholesterin, etc.—purins, and certain other compounds has been very little studied. At the present writing the question of requirements for growth is under active investigation; until we have more complete data it is best to be very cautious in making scientific laboratory investigations the basis of any radical changes in the dietaries dictated by custom and instinct.

The amount of **carbohydrate** and **fat** in the food varies more than the amount of protein. Carbohydrate and fat are utilized to produce energy that is turned into work and heat, and the amount needed depends on the amount of work to be done and on the climate; in a cold climate or when much work is done more carbohydrate and fat are needed. There is, however, a certain minimum of energy developed even at rest. The body of the warm-blooded animal is constantly giving off heat by conduction and radiation, in the urine and feces, and in the evaporation of water from the skin and lungs. If an animal is not to lose weight it must be given enough food to furnish energy for the work done as

well as to cover that lost as heat. The amount of heat developed when at complete rest depends entirely—or nearly so—on the surface area of the animal, so that even when an animal is at rest there is a minimum of energy to be supplied. A curious fact has been discovered: if the heat given off by a starving animal at rest—the so-called basal requirement, equal to about 1000 calories in a 140 pound man—is determined, then foodstuffs enough given to just cover this requirement, more heat is given off than the basal requirement; the food itself stimulates the metabolism and causes an increased heat formation. If we give food equivalent to 1000 calories to a man whose basal requirement is 1000 calories he will give off 1300 calories if the food is protein, 1130 if it is fat, and 1060 if it is carbohydrate. This is the so-called specific dynamic effect—30 per cent. for protein, 13 per cent. for fat, 6 per cent. for carbohydrate. It is somewhat similar to what takes place when we try to bring about nitrogen equilibrium by administering the amount of nitrogenous food just equivalent to the amount of nitrogen excreted by a starving individual; the nitrogen excreted in this case increases and equilibrium is not reached.

Carbohydrates are broken down in the gastro-intestinal tract to simple monosaccharides, like glucose, and absorbed as such. If not oxidized at once to carbon dioxide and water to give energy, carbohydrate may be stored in the muscles or liver as glycogen or changed to fat and stored as such. A small amount of glycogen is stored in the muscles to be used as a source of muscular energy. An excess over that needed in the muscles is stored in the

liver and serves as a reserve to replenish the glycogen store of the muscles as this supply becomes used up. If there is a great excess of carbohydrate, more than needed to replenish the whole glycogen reserve of the body, it may be changed to fat and stored as such. The amount of glycogen in the body depends on the state of nutrition. If a dog is starved for a day or two all his glycogen will be used up and the reserve of fat drawn on for the production of energy. The length of time a starving animal will live depends chiefly on the amount of fat in the body; the glycogen is used up in a day or two, then, in a lean animal, the protein breaks down; if the animal is fat, the fat spares part of the body protein. The store of food material may be compared with an individual's wealth: the muscle glycogen can be compared with the small change in the pocket-book; the liver glycogen with the ready money available in the bank; and the fat with the stocks, bonds, and real estate used only in times of great need. The amount of carbohydrate in the diet is very variable and depends on the amount of work done; with very light work 500 grams a day is sufficient. Carbohydrate cannot be entirely replaced by fat: for some unknown reason, when carbohydrate is omitted from the food, the food fat is not completely oxidized to carbon dioxide and water; a certain amount is not oxidized beyond $\beta$-oxybutyric acid, and the patient suffers from acidosis.

**Fat** is broken up in the gastro-intestinal tract to glycerin and fatty acid and absorbed as such; it may then be oxidized at once to produce energy and be excreted as carbon dioxide and water or it may be stored as fat; in the latter case it serves

as an insulator protecting the body from loss of heat. On account of its high heat value fat is much used as a food in cold climates. Body fat, then, comes partly from the fat in the food, partly from the carbohydrates and partly from the protein.

Protein food is used in part to replace tissue waste and in part as a soure of energy; in so far as it is used as a source of energy it may be replaced by isodynamic quantities of fat or carbohydrates—1 gram of protein is equivalent to 4.1 calories, 1 gram of carbohydrate to 4.1 calories, 1 gram of fat to 9.3 calories. It may not be strictly true that the distinction between the metabolism of protein food on the one hand and that of fat and carbohydrate on the other is as sharp as we have sometimes believed. It has been pointed out that fat and carbohydrate serve as a source of energy and that albuminous food can serve not only as a source of energy but also as a source of material for the formation of living body tissue. There is, however, some evidence that certain amino acids which may serve as a basis for protein formation can be synthesized from ammonia and non-nitrogenous organic compounds and that the non-nitrogenous compounds may come from the carbohydrates or fat of the food. The truth may, therefore, be that though the nitrogenous part of the body protein can come only from the protein food, the non-nitrogenous part of the protein food is qualitatively more nearly equivalent to carbohydrate and fat, in that all of these may serve not only as a source of energy, but, after combination with nitrogenous compounds, as a source of body protein as well.

Many different methods have been used to study

the intermediary metabolism—the changes which amino acids, glucose, glycerin and fatty acids undergo after absorption and until they are excreted as simple end products—but the subject is still obscure.

## Pathological Part.

### Malnutrition.

Patients may be weak, thin, anemic, and generally run down for various reasons; lack of sufficient food—which, in turn, may be due to a variety of pathological, physiological, psychical, or, even, social reasons—may be responsible; improper digestion, losses through gastro-intestinal fermentation, putrefactive, or other intestinal parasites, or some disturbance of secretion or absorption may be responsible; or some constitutional or infectious disease or other disturbance of the general metabolism leading to improper utilization of the food. No general rules for treatment can be laid down; the treatment depends upon (1) recognition, so far as possible, of the causes of the faulty nutrition; (2) a knowledge of the fundamental principles of metabolism; and, lastly, success in treatment depends very largely on (3) the psychic element, the skill with which knowledge of the principles is applied.

Insufficient food is sometimes responsible; in such cases the indication is for more food, but it may require considerable ingenuity to get the proper amount of food into the patient. Instruction to eat more may suffice; but sometimes the lack of appetite amounts to a very strong distaste for all food. Well cooked food is one of the best appetizers; bitters—

such as nux vomica, gentian, capsicum, bitter alcoholic drinks such as vermouth—may be useful. The psychic side of eating is very important. Attention to various details of the service and manner of eating help. It is not uncommon to find that travellers who have considerable trouble with the appetite and digestion when away from home and obliged to eat at hotels, are free from such disturbances when at home; eating slowly in congenial company and with a pleasant environment when at home is in part responsible for the difference. More exercise, more fresh air, a change of scenery or surroundings often serve to improve the nutritive condition. Fat has a high caloric value and, in undernourished individuals, can often be increased with good results, but it is not always well borne and may give rise to gastro-intestinal disturbances when taken in excess; by proper methods of administration, the amount taken can often be greatly increased without giving rise to any ill effect. Butter, cream, and olive oil are well borne and easily absorbed; large quantities of oil can be used on salad, large quantities of cream can be taken in coffee, with baked apple, or cereal, or as a drink after meals. It may sometimes seem advisable to prescribe alcoholic drinks for their food value. Alcohol is largely oxidized in persons accustomed to its use and has a high caloric value—7.0 calories per gram; a drink of whiskey, for example, about 30 grams, with 50 per cent. alcohol gixes ($15 \times 7 =$) 105 calories, equivalent to ($105 \div 9 =$) 12 grams fat. The alcohol acts also as an appetizer. It may, furthermore, decrease oxidation processes and so lead to a storing up of some of the other foodstuffs. The poisonous effect of the alco-

hol should, of course, not be overlooked. Its use as a food may be compared, in certain respects, to the use of dilute hydrochloric acid to run a steam engine: the dilute acid can, of course, be used for a time instead of water, but it corrodes the engine.

If there is any suspicion that poor absorption is responsible for the undernutrition arsenic can be given. Plenty of water with the meals is believed to aid absorption. Poor absorption of fat may sometimes be improved by the administration of bile or pancreatin. Any other disturbance of secretion or absorption in the gastro-intestinal tract should be treated. Sometimes, there seems to be a low metabolic capacity; hydrotherapy—both hot baths and cold baths increase the metabolism—and other general hygienic measures sometimes help this; a patient will sometimes gain in weight by taking up systematic gymnastic exercises.

Undernutrition is often a condition accompanying other diseases rather than a disease by itself, but it is sometimes the principal feature of the disease to be treated; it may be that the accompanying disease is responsible—in part at any rate—for the malnutrition; it may be that the malnutrition is a contributory factor to the accompanying disease: the relation is frequently one leading to a vicious circle, each factor making the other worse. In cases of pulmonary tuberculosis, for example, malnutrition is usually one of the striking features and one to which most attention is directed in treatment, since the length of life often depends on the capacity to digest and absorb. This condition is a good example of the importance of function rather than anatomical change for treatment; the patho-

logical change is in the lungs, but in treating we devote our attention in great part to the gastro-intestinal tract and let the local condition in the lungs take care of itself. Anemia and malnutrition are often associated; in such cases both the anemia and the malnutrition should be treated. And, similarly, in many other conditions, the treatment of malnutrition comes under the heading of treatment of the gastro-intestinal tract.

## Obesity.

When an excess of food over that oxidized by the body is taken, the excess may be stored as fat. Obesity may be due to eating too much, to exercising too little, or to a constitutional tendency to low oxidation. Ordinary observation shows great individual differences in the tendency to lay on fat; this may depend on a difference in the capacity to oxidize food material. If two persons each take the same amount of food one may oxidize it all, the other may oxidize only a part of it and store the rest as fat. A sedentary life free from care may lead to accumulation of fat; a very active life in the open air tends to more complete consumption of foodstuffs. Farmers, hunters, and laborers who lead an active life in the open air are, on the whole, not inclined to obesity. Elaborate calorimetric studies have recently demonstrated that the basal metabolism of different individuals of the same shape, size, and weight is different; that men, for example, have a more active metabolism than women; and that trained athletes have a more active metabolism than untrained men. Long continued use of alcoholic drinks may lead to obesity—partly because alcohol

spares some of the foodstuffs and partly, perhaps, because the drug may depress the oxidizing capacity of the tissues. A tendency to low oxidizing capacity and obesity is frequently hereditary.

By increasing the amount of tissue to be nourished, marked obesity makes more work for the heart, and, if the heart itself is affected, may diminish its efficiency; the patient may suffer from dyspnea, congestion of the organs and even Bright's disease.

The general principles of treatment are theoretically simple. We can decrease the amount of food, increase the amount of work the patient does, and, to a certain extent, can influence the capacity to oxidize. But the actual carrying out of the treatment often presents great practical difficulties. Exercise is often difficult, sometimes even dangerous, for a very fat person; and partial starvation, which is the basis of all the dietetic methods of treatment, is very difficult to enforce. Complete starvation leads to the consumption of the body protein as well as the fat; the patient loses strength and the heart muscle may undergo degeneration. While generally considered not very safe, treatment of obesity by repeated, complete, but not too long fasts—controlled by examination of the urine for acetone bodies—has been tried recently in a few cases and found successful.

In most forms of dietetic treatment protein is decreased; fat is usually decreased but may not be; it may, in fact, be increased. The table shows typical forms of diet for the treatment of obesity.

| | Protein | Carbohydrate | Fat | Calories |
|---|---|---|---|---|
| Normal Diet ........ | 100 | 500 | 50 | 3000 |
| Banting (English) ... | 175 | 50 | 8 | 1100 |
| Ebstein (German) | 100 | 50 | 85 | 1300 |
| Hirschfeld (German) | 115 | 110 | 45 | 1300 |
| Oertel (Austrian) .... | 100 | 100 | 35 | 1100 |
| Robin (French) ...... | 140 | 80 | 45 | 1300 |

The Banting and Ebstein diets were prescribed empirically before modern metabolism studies had been made. By decreasing the carbohydrate, not only do we withdraw this amount of food from the diet, but the absence of carbohydrate makes it difficult to eat much other food. The large quantity of protein in the Banting diet is supposed to prevent the patient from losing strength and having a nervous breakdown; anemic patients are said to stand it well. In the Ebstein diet the fat is somewhat increased in the belief that it stays longer in the stomach and so allays somewhat the feeling of hunger. These different dietetic cures for obesity need not be learned in detail. The important points to bear in mind are: (1) that the carbohydrate should be greatly diminished; (2) that the protein should not be too greatly decreased. The secret of success lies in properly choosing the foodstuffs and managing the patient psychically. All the methods are starvation methods and the patient feels hungry; he should, therefore, be given bulky, filling foods of low caloric value—green vegetables, fruits, etc.

A special form of starvation cure—a diet of milk alone—recommended by Karell is especially valuable in cases with heart or kidney complications. In the modification of the treatment as worked out by Moritz, the patient is given milk equivalent to 16 or 17

calories per kilogram of the weight which he should have for his height. Thus the normal weight for a man 32 years old, and 170 centimeters high, is about 70 kilograms; such a patient should be given milk equivalent to about $(16.5 \times 70 =)$ 1150 calories—about 1600 grams; 1600 grams of milk contain 64 grams protein (=263 calories), 64 grams fat (=595 calories), 64 grams carbohydrate (=263 calories)—1120 calories in all. A skimmed milk diet is sometimes given; three liters of skimmed milk is equivalent to about 1035 calories and contains 120 grams protein, 190 grams carbohydrate, and 20 grams fat.

Alcoholic drinks should be forbidden or very much restricted; alcohol acts in two ways, as a food, and, also, as a method of decreasing the capacity for oxidation; abstinence from all alcoholic drinks, furthermore, in persons accustomed to its use, often serves to greatly diminish the appetite.

Oertel lays great stress also on restricting the consumption of water and other liquids, especially in cases in which there is retention of fluid and hydremia; restricting fluids serves also to decrease the appetite. Cathartics, especially the hydragogue cathartics, are used to deplete the system and to decrease absorption of foodstuffs.

Fat persons should also be encouraged to exercise as much as they can without damage to the heart. Increasing the amount of work done may increase the appetite, but this increase in the appetite should not be satisfied by increasing the food. The exercise acts in two ways; it not only directly increases food consumption, but also often increases the capacity for oxidation. Cold baths and hot baths also increase the metabolism, and various

forms of hydrotherapy, especially hot baths, are, therefore, often useful.

Thyroid extract is sometimes used to increase the activity of the metabolism. It is very effective, but should be used with great caution. It may cause destruction of nitrogenous body tissue and may affect the heart; to combat the effect on the heart, digitalis may sometimes be given at the same time. On account of the loss of nitrogen, somewhat more than the normal amount of protein should be given in the food. To bring about a rapid loss of weight at the start, and so encourage the patient to persist with the rather trying dietetic treatment, thyroid extract is sometimes given in combination with dietetic treatment in the beginning. If the loss of weight is too rapid, or the patient complains of dizziness, headache or nervousness as the result of the thyroid treatment, the amount of thyroid should be decreased.

## Fever.

Since a discussion of the principles of treating fever deals largely with methods of influencing the metabolism, a strict adherence to the principles of classification adopted throughout would bring the discussion of fever and its treatment at this point; but for practical reasons it seems better to discuss the subject under the specific infectious diseases.

## Diabetes.

**The metabolism in diabetes.** In a patient complaining of progressive emaciation in spite of voracious appetite, great thirst, and, possibly, cutaneous symptoms—itching, eczema, boils, carbuncles—ex-

amination of the urine will frequently show evidence of diabetes. In this condition the body is unable to oxidize sugar normally and the glucose becomes excreted in the urine as an end product of metabolism. Not only the glucose from carbohydrate food is excreted, but, in severe cases, more than half the protein of the food may be changed to glucose and become excreted as such. In very severe cases there is evidence of formation of sugar even from fat; in such cases, furthermore, fat may be incompletely oxidized and appear in the urine as $\beta$-oxybutyric acid. These losses of foodstuffs make it easy to understand the emaciation and enormous appetite characteristic of diabetes; the polyuria accounts for the great thirst. The tendency to infection of the skin may be associated with the increased sugar content or some other chemical change in the tissue fluids that make them less resistant. The coma that often closes the life of the patient is believed to be due to the enormous drain of alkalies consequent on the increased formation of acid from fat.

The presence of sugar in the urine is not always a sign of diabetes. The sugar may not be glucose; a pentose is occasionally found; and, in nursing women, sometimes, lactose. The presence even of glucose does not always indicate diabetes; a transient diabetes may be found after certain drugs and under a number of different conditions.

Glycosuria is usually due to hyperglycemia. Normally the carbohydrates of the food are split in the intestine into monosaccharides like glucose and absorbed as such into the blood. The glucose is carried by the portal circulation to the liver and the greater

part of it stored there in the form of the polysaccharide glycogen, only to be broken down again as fast as the tissues need it. The circulating blood contains about 0.1 per cent. glucose. This glucose is taken up by the tissues; as fast as the glucose of the blood is used up and its concentration in the blood tends to decrease, more glucose is formed from the glycogen of the liver so that the amount in the blood is kept at a constant level. The urine does not normally contain glucose, but if, for any reason, the content of the blood in glucose increases above 0.1 per cent. the excess is at once excreted through the urine. Any conditions leading to this hyperglycemia can be responsible for glycosuria.

Glycosuria without hyperglycemia is possible. Such a condition occurs after the administration of phloridzin. It is believed that phloridzin increases the permeability of the kidney for glucose so that glucose is excreted even when the blood contains no more than the normal amount of glucose. One explanation given is that glucose does not exist free in the blood but combined with some colloidal substance, that the phloridzin splits the glucose-colloid compound setting the glucose free, and that the kidney is permeable for the free glucose. There is no known spontaneously occurring clinical condition resembling phloridzin diabetes, that is, glycosuria without hyperglycemia; but the condition of artificial phloridzin diabetes is, nevertheless, of importance, for it is extensively used in experimental studies of the intermediary metabolism of carbohydrates.

The clinical forms of glycosuria are believed to be always due to hyperglycemia. We can imagine

different causes for the hyperglycemia. If we tabulate the various steps of glucose metabolism so far as they relate to the glucose of the blood, we have

(1) the introduction of glucose from the gastro-intestinal tract into the blood;

(2) the disappearance of glucose from the blood resulting from the formation of glycogen in the liver—**glycogenesis**;

(3) the re-introduction of glucose into the blood resulting from the breaking down of glycogen in the liver—**glycogenolysis**;

(4) the disappearance of glucose from the blood and its oxidation in the tissues—**glycolysis.**

Hyperglycemia may result from a disturbance of any one of these four functions.

If large quantities of easily absorbable sugar are eaten, glucose may be introduced into the blood faster than it disappears into the liver as glycogen and so give rise to hyperglycemia. Ordinarily, most of our carbohydrate food is ingested as starch; this is only slowly changed to glucose and absorbed little by little; but if, in a short time, we eat a large quantity of easily absorbable sugar—say a pound or more of candy containing easily hydrolized cane sugar, and, perhaps, also glucose—glucose may be absorbed so very rapidly and pass through the liver in such large quantities that some of it may escape storage in the liver and the resulting hyperglycemia may result in what is called alimentary glycosuria. There are considerable individual differences in the amount of carbohydrate that can be ingested before the onset of alimentary glycosuria. The condition can, of course, be easily distinguished from a real diabetes.

We can imagine a condition of hyperglycemia resulting from increased glycogenolysis—an increase in the rate of glucose formation from glycogen without a corresponding increase in sugar oxidation. Such a condition may be brought about by injection of epinephrin, extract of the posterior lobe of the hypophysis, thyroid extract, and possibly extract of other glands of internal secretion. Puncture of the floor of the fourth ventricle, which has long been known as a cause of glycosuria, probably acts by leading to hypersecretion of epinephrin and, therefore, indirectly causing increased glycogenolysis. Such methods are effective in causing glycosuria only when the liver contains glucose; they are ineffective in a starving animal. There are occasionally clinical forms of glycosuria which may be associated with pathological changes in the adrenals, the thyroid, the hypophysis, or the "sugar center."

Finally, there is the possibility of hyperglycemia as a result of decrease in the rate of removal of glucose from the blood and oxidation in the tissues; such a condition occurs when the pancreas is removed. In this case glucose accumulates in the blood because the tissues lose their power to oxidize glucose. It has been demonstrated experimentally that the heart of a dog from which the pancreas has been removed is unable to oxidize sugar like the normal; and that the power to utilize sugar can be restored by the addition of boiled extracts of pancreas to the nutrient fluid bathing the heart. The spontaneously occurring clinical form of diabetes, diabetes mellitus, seems to resemble pancreatic diabetes in that the trouble lies in an inability on the part of the tissues to utilize glucose and properly oxidize it.

Whether or not the pancreas is always diseased in diabetes mellitus we do not know; in a large portion of diabetics the pancreas shows degenerative or inflammatory changes especially in the Islands of Langerhans—these latter probably glands that have an internal secretion which has something to do with the oxidation of glucose in the body.

In severe cases of diabetes the metabolism not only of carbohydrates but also of protein and fat may be disturbed. Protein can serve as a source of glucose and, in severe forms of diabetes, sugar may appear in the urine on a free diet from carbohydrates. It has already been pointed out that proteins are split up in the intestine to their simple amino-acid constituents. These are absorbed and partly utilized by the tissues to replace wear and tear. From some of the amino-acids the nitrogen is removed and excreted, leaving a carbonaceous nitrogen-free residue that may be changed to glucose. The amount of glucose that can be derived from protein can be determined by feeding meat to a dog from which the pancreas has been removed or to a dog to which phloridzin has been administered. In such animals the glucose formed from protein will not be oxidized but will appear in the urine and can be measured quantitatively. A simultaneous determination of the nitrogen in the urine shows how much protein has been destroyed to form this amount of sugar. Experiments of this kind show 3.65 grams of dextrose for each gram of nitrogen in the urine. Since one gram of nitrogen corresponds to 6.25 grams of protein, or approximately 250 calories, and 3.65 grams of dextrose to approximately 150 calories, the loss of protein energy in the

form of dextrose in pancreatic diabetes, may, therefore, be nearly 60 per cent. If to this loss we add the amount of energy lost as specific dynamic effect —namely, 30 per cent. in the case of protein—we find that nearly 90 per cent. of the energy of protein food may not be available in severe diabetes. Furthermore, fats may be incompletely oxidized, being excreted, in part, as $\beta$-oxybutyric acid, so that some of the energy of the fat of the food is lost. These are the theoretical possibilities in a severe enough case of diabetes. As a matter of fact, most patients die before reaching such a severe stage of the disease; but as an illustration of the great loss of energy in an actual case, one studied by Magnus-Levy may be reported. The patient was a boy who was unable to utilize carbohydrate; to cover his energy requirement, estimated at 1650 calories, it was necessary to give him 2278 calories as protein and fat; the diet was made up of 90 grams protein, equivalent to 369 calories; 200 grams fat equivalent to 1909 calories. Ninety-seven and five-tenths grams of $\beta$-oxybutyric acid, corresponding to 443 calories; 50 grams of glucose, corresponding to 185 calories (628 calories in all) were excreted in the urine. From this we see one of the tasks in therapeutics, namely, to administer enough nourishment for the patient.

Another complication that may result from the formation of $\beta$-oxybutyric acid in severe diabetes is acidosis.

The reactions of living matter take place only in a medium that is practically neutral. In spite of a continuous production of carbonic and sulphuric acid—from the oxidation of carbon and sulphur

compounds respectively—and other acids in the metabolism, this neutral reaction in the blood and tissue fluids is maintained within very narrow limits by the continuous excretion of the acid end-products through the lungs and kidneys,—the volatile carbonic acid through the lungs, the non-volatile acids through the kidneys. There is, moreover, a mechanism for preventing these compounds from exerting their harmful acid properties even while in the body and during transportation from the cells, where they are formed, to the organs of excretion. This consists in the presence of two pairs of compounds, either of which pair alone is a nearly perfect mechanism for maintaining neutrality. One of these pairs is made up of acid phosphate, $NaH_2PO_4$ (or $KH_2PO_4$) and alkaline phosphate, $Na_2HPO_4$ (or $K_2HPO_4$) the other of carbonic acid $H_2CO_3$, and bicarbonate, $NaHCO_3$ (or $KHCO_3$); (for the sake of simplicity only the sodium compounds will be referred to.) Such mixtures have the peculiar property of being able to neutralize large quantities of either acid or alkali without perceptibly changing in reaction. As the result of a very small amount of free H ions coming from a slight dissociation of one of the hydrogens in the $H_2PO_4$ ion ($H_2PO_4 = HPO_4 + H^+$), acid sodium phosphate in aqueous solution is a very weak acid. As the result of a very small amount of OH ion coming from a slight reaction between the $HPO_4$ ion (this comes from the dissociation of $Na_2HPO_4$,—$Na_2HPO_4 = 2Na^{++} + HPO_4^{--}$) and water ($HPO_4 + HOH = H_2PO_4^- + OH^-$), alkaline sodium phosphate, in aqueous solution, is a very weak base. If solutions of these two substances, alkaline phosphate and acid

phosphate—one a very weak base, the other a very weak acid—are mixed, they practically neutralize each other so that, even though the amount of one is in slight excess in such a mixture, the acid and basic properties of the two substances are so slight even when alone that the mixture is neutral.* In other words, a mixture of these two substances, even in very unequal proportions, is practically neutral. The reason that either strong acid or strong alkali can be added to such a mixture without changing the neutral reaction is that acid, on the one hand, merely changes some of the alkaline sodium phosphate to acid phosphate according to the reaction,

$$Na_2HPO_4 + HCl = NaH_2PO_4 + NaCl;$$

and alkali, on the other hand, merely changes some of the acid sodium phosphate to alkaline sodium phosphate according to the reaction,

$$NaH_2PO_4 + NaOH = Na_2HPO_4 + H_2O;$$

the end-result in either case being merely a change in the relative proportion of the two substances in solution. But, as already stated, a mixture of the two substances, even in very unequal proportions, is still practically neutral. A mixture of sodium bicarbonate and carbonic acid has neutralizing properties similar to the mixture of phosphates. In the blood and tissue fluids there is, therefore, a double

* This statement, though lacking somewhat the precision of a more extended quantitative statement of the properties of such a mixture made with the aid of Ostwald's dilution formula and the mass action law of Guldberg and Waage, is, nevertheless, substantially correct, and will be more intelligible to the physician who may know but little of physical chemistry.

mechanism for the maintenance of neutrality. This double mechanism serves to absorb all acid normally formed in the body without permitting a change in the reaction of the fluids. The best relative proportions of these four substances is maintained, and an undue accumulation of the acid members of the two pairs prevented, by the continuous excretion of carbon dioxide through the lungs and acid phosphate through the kidneys.

The mixture of phosphates and carbonates, together with the continuous excretion of the acid members of these two pairs of substances, is, so far as we know, the only mechanism for the maintenance of neutrality in herbivora; for this reason, a starving herbivorous animal succumbs to acidosis fairly easily, following acid administration—the alkali supply soon becoming exhausted. In carnivora there is an accessory mechanism, and these animals, therefore, stand acid administration much better. The chief end-product of nitrogenous metabolism in carnivora is ammonia, and this is used, so far as needed, to neutralize acid; urea is formed only from ammonia formed in excess of what is needed to neutralize acid. This explains why it is that the amount of ammonia excreted in the urine serves as such a good index of the degree of acidosis.

The acidosis in severe diabetes is due to the formation of excessive quantities of $\beta$-oxybutyric acid, and this compound, together with diacetic acid and acetone, which are derived from it by simple chemical changes, may be found in the urine.

$$
2\begin{array}{l} CH_3 \\ | \\ CHOH \\ | \\ CH_2 \\ | \\ COOH \end{array} + O_2 = 2\begin{array}{l} CH_3 \\ | \\ CO \\ | \\ CH_2 \\ | \\ COOH \end{array} + 2H_2O \qquad \begin{array}{l} CH_3 \\ | \\ CO \\ | \\ CH_2 \\ | \\ COOH \end{array} = \begin{array}{l} CH_3 \\ | \\ CO \\ | \\ CH_3 \end{array} + CO_2
$$

$\beta$-OXYBUTYRIC ACID — DIACETIC ACID — ACETONE

B-oxybutyric acid is derived from fat. For some unknown reason, when fat alone is oxidized in the body without the simultaneous oxidation of carbohydrate, the oxidation of the fat is incomplete; instead of reaching the stage of carbon dioxide and water some of it becomes oxidized only to the stage of $\beta$-oxybutyric acid. Even in such cases the mixture of phosphates and carbonates serves to maintain the neutrality of the blood and tissues; but as a result of the rapid formation and excretion of the abnormal acid in the form of salt, much alkali is lost from the body and the amount of sodium bicarbonate in the blood becomes very low. Since the carbon dioxide is transported from the tissues to the lungs largely in combination as sodium bicarbonate, a decrease in the amount of this latter substance means a decrease in the power of the blood to transport carbon dioxide. Carbon dioxide then accumulates in the tissues, and the result is a form of internal suffocation which, if not relieved, results in death. This kind of acidosis, due to the formation of increased quantities of $\beta$-oxybutyric acid, may occur occasionally in other conditions—starvation, pernicious vomiting—where fat alone without carbohydrate is undergoing oxidation.

A less marked degree of acidosis of a somewhat different form is sometimes observed as a result of

retention of normal acid end-products of metabolism in cases of nephritis.

**Treatment.** Since we do not know the cause of diabetes, we cannot treat it by direct methods which aim at restoration of the anatomical integrity of the diseased organs. At present, we can say little more than that hyperglycemia is present as a result of the inability of the tissues to oxidize glucose. Since the body cannot oxidize glucose, the nutrition must be maintained chiefly by other foodstuffs. The treatment is chiefly dietetic: rigid rules cannot be laid down; the exact details vary with different patients and with the same patient at different times. It should be borne in mind that diabetes resembles many other chronic diseases in that it is not a condition with an inherent downward tendency but a weakness of function compatible with life and a certain degree of efficiency if the amount and kind of food administered is kept down below the limits that the patient can properly metabolize. The same general principles used in the treatment of other chronic diseases are used in treating diabetes. The power of the tissues to utilize and oxidize certain foodstuffs, especially carbohydrates, being diminished, the amount of these foodstuffs administered is, therefore, decreased to that which the body can oxidize; and, at the same time, the power of the tissues to oxidize carbohydrates is stimulated and improved by a special system of metabolic training. In all modifications of the dietetic treatment of diabetes, the carbohydrate food is decreased to the amount that the patient can oxidize; and the power of the tissues to oxidize carbohydrates is gradually increased by slowly

adding small amounts of carbohydrate food, always keeping within the limits of what the body can oxidize. Emphasis has recently been laid on graduated muscular exercise as a means of increasing the power of the body to oxidize carbohydrates. In addition, the nutrition of the patient must be maintained, and this in spite of the fact that the capacity to utilize foodstuffs is diminished; and the various symptoms, especially acidosis, must be combated.

As in other forms of chronic disease, the severity of the disease is the chief factor taken into consideration in the therapeutic classification. Diabetes may be divided into four classes,—light, moderate, severe and very severe. Light cases can stand a small amount—two to four ounces—of carbohydrate food in the diet without showing glucose in the urine. Cases of moderate severity show glucose in the urine when any carbohydrate at all is administered, but do not show glucose when no carbohydrate is administered. Severe cases are those in which glucose is excreted even on a diet free from carbohydrates, sugar being formed from protein. Among these latter, a group of very severe and rapidly fatal cases may be separated in which 3.65 grams of glucose appear in the urine for each gram of nitrogen—an indication that all the sugar formed from protein is excreted in the urine. To distinguish between mild and moderate cases, Von Noorden has recommended a standard diet which is much used; the patient is given 50 grams bread for breakfast and lunch and, in addition, if desired, meat, eggs, green vegetables, cheese, coffee and wine. If the urine remains sugar-free, the diabetes is mild in character.

When a patient is found to have diabetes, the carbohydrate in the food can be reduced either rapidly or gradually. Physicians are not entirely agreed on this point; it depends somewhat on the case. In a patient excreting large quantities of urine and showing marked subjective symptoms, the prompt disappearance of the symptoms following an abrupt change to a strict carbohydrate-free diet may have a very good psychical effect. In such cases the urine should be examined for diacetic acid and acetone and the patient carefully watched for symptoms of coma. If it seems desirable to omit all carbohydrate food at once, 500 grams of meat per day with some fat and, perhaps, some carbohydrate-free green vegetables may be given and nothing else, and the urine examined from day to day until it is free from sugar. If the urine becomes sugar-free the diet may be kept up for a week afterwards and then food containing one ounce of carbohydrate added. If the patient stands one ounce of carbohydrate a day without showing glucose in the urine, another ounce may be added; the carbohydrate food should not be given all at once but should be divided over the three meals. In this way the amount which the patient tolerates can be determined and the amount in the diet kept within it. The amount of carbohydrate food in the diet should be kept somewhat below that which the patient can tolerate; if he can tolerate four ounces, but not 4 1-2, without showing glucose in the urine, he should be given not more than about three ounces a day for a week. If his tolerance is again determined at the end of this time, it may be found to be 6 or 7 grams; the patient may then be given 5 grams a day for a long

period. By resting and training the cells for long periods in this way at a level somewhat within their capacity they can sometimes be gradually trained to increase their power to oxidize carbohydrate. Cases occasionally occur in which the cells can be trained to take a full normal carbohydrate diet. The treatment is difficult to carry out. It requires honesty, self-denial and intelligent co-operation on the part of the patient. Diabetic patients have a great craving for carbohydrate food and will often lie to the physician and get carbohydrate by stealth.

In selecting foodstuffs for diabetic patients the important factor is the carbohydrate content. In general, meat (except liver), fish (except oysters), and eggs contain little or no carbohydrate, and the foodstuffs from the vegetable kingdom, except the various green vegetables, like lettuce, celery and spinach, contain carbohydrates. But guesses regarding food composition should not be made; in every case the composition should be looked up if it is not known; unless this is done, serious mistakes will be made. Diabetic patients are not infrequently told that they may have skimmed milk but not cream in the belief that cream is too "rich" a food for them; such advice is wrong, since skimmed milk contains much more sugar compared with its total caloric value as a food than cream. This is simply one example of the kind of mistakes that result from guessing at the composition of foodstuffs. For sweetening purposes saccharine, a sweet substance which is not a carbohydrate, may be used. The various so-called carbohydrate-free gluten breads should be used only with caution; they generally contain as much, or nearly as much, starch as wheat

flour. Cream is very nutritious and easily taken, and a quart of cream contains only a little over an ounce of sugar. While the carbohydrate content is the important factor in determining the advisability of any foodstuff for a diabetic patient, it is not always strictly true that the amount of glucose in the urine of a patient varies with the carbohydrate content of the food. Sometimes two foodstuffs with equal carbohydrate content will give very different results in this respect and for absolute certainty it is, therefore, necessary to examine the urine of each patient to determine how he reacts to each foodstuff. Indeed, the administration of certain foodstuffs rich in carbohydrate (oatmeal, potato) is sometimes attended with very favorable results.

On account of the lowered capacity of the body to utilize foodstuffs, the patient should decrease his activities both physical and mental; the condition is not compatible with great muscular activity, and clinical experience shows that excitement, worry, and other emotions make the condition worse. It has been demonstrated that excitement and other forms of undue mental activity often cause hyperglycemia: a transient glycosuria often occurs in students as the result of a severe examination; and analysis of the urine of the members of a large football squad after a game has shown glycosuria in about half of them which, since some of them were only substitutes and spectators, must have resulted simply from the excitement of the game. There is some clinical evidence that such factors may, perhaps, be of importance in the etiology of diabetes. In regard to the amount of muscular exercise advisable it is sometimes not easy to decide

without experiment. The decreased power to oxidize carbohydrate makes it necessary to economize the activities and so husband the resources of energy. In light and moderate cases, on the other hand, graduated muscular exercises are sometimes followed by an increase in the power to oxidize carbohydrate. Exercises should be restricted if, as indicated by increase in the nitrogen excretion, there is evidence of breaking down of muscular tissue. Especial attention should be directed to keeping the skin clean, for diabetic patients are very susceptible to infections of the skin.

The severe cases are especially difficult to treat. Carbohydrates are bad for the patient; he cannot utilize them and they make the condition worse. On a diet of protein and fat alone there is danger of incomplete oxidation of fats and the consequent formation of the acid end products which bring on coma. Furthermore, the absence of carbohydrates from the diet may lead to gastro-intestinal disturbances, especially intestinal putrefaction. Finally, it is very difficult to stand such a diet; the craving for carbohydrate food may be very great. If the patient loses very much weight on a carbohydrate-free diet or if intestinal putrefaction occurs it may be necessary to add a little carbohydrate; since the action of the putrefactive organisms on protein takes place only when the reaction is alkaline, the various acid end products resulting from the fermentation of a small amount of carbohydrate in the intestine may prevent intestinal putrefaction. A small amount of carbohydrate food may have to be given to prevent the onset of acidosis. Acidosis is combated also by the administration of large quantities of alka-

lies. If, for any reason, a diabetic patient cannot be kept permanently on a diet strict enough to keep the urine glucose-free, he should be put on such a diet from time to time at least—starved, even, if necessary.

Certain investigators lay great stress on the value of fasting in the treatment of diabetes. They say that more emphasis should be laid on the fact that diabetes is a weakness of metabolic function in which the metabolism of protein and fat is involved as well as that of carbohydrate: in the milder grades there is a decreased capacity to metabolize carbohydrate; in severe types of the disease the capacity to metabolize protein and fats as well may be decreased; and this explains the necessity for abstaining from foods other than carbohydrates and the good results obtained by this treatment. In carrying out the treatment, the patient is starved for a period of from one day to a week or more until the urine becomes free from glucose. When feeding is again begun, one new article of food at a time is given, beginning with foodstuffs poor in carbohydrates, though less stress is laid on the carbohydrate content than in the older forms of treatment. Bulky, filling foodstuffs, especially the green vegetables, are much used. The amount and variety of foodstuffs is gradually increased up to the amount that a patient can tolerate without excreting glucose. The urine is tested daily and if glucose appears, a day or two of starvation is introduced until the urine is again sugar-free. During the starvation periods alcoholic drinks may be given if necessary; alcohol has a certain nutritive value, it may prevent acidosis, and does not give rise to glu-

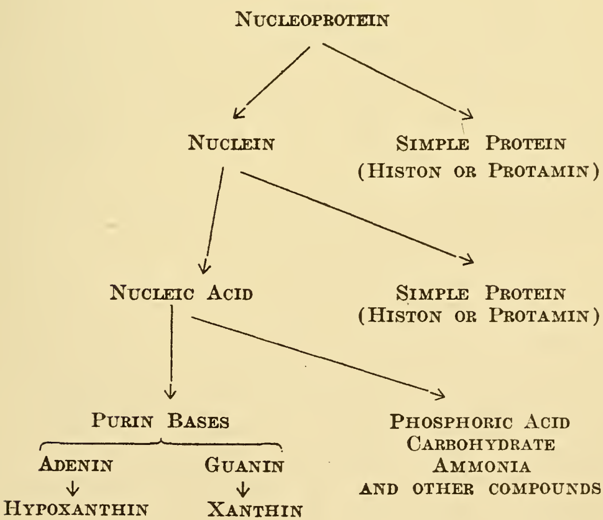
cose in the body. Sodium bicarbonate may also be given to prevent acidosis. The results of this form of treatment have been surprisingly successful.

## Gout.

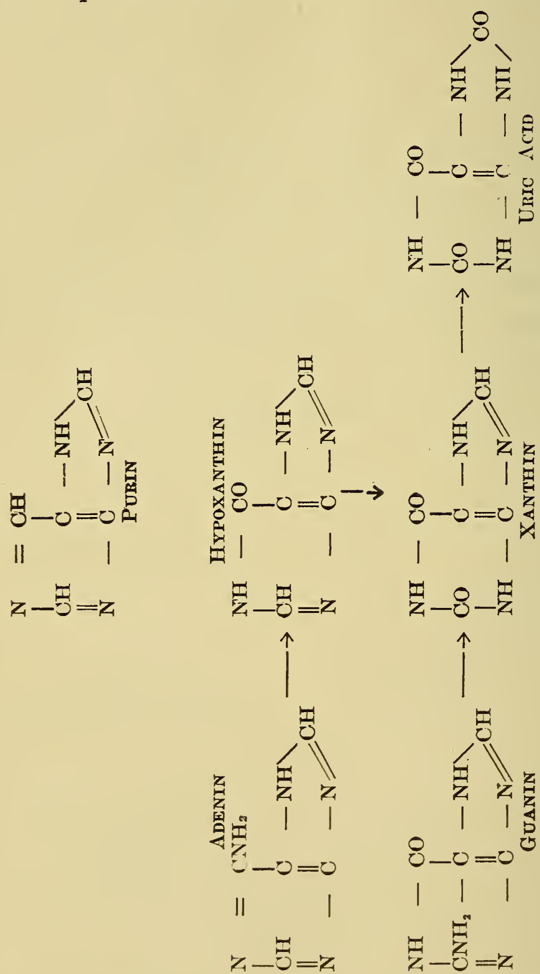
Gout is distinguished from the other chronic arthropathies chiefly by the clinical history—monarticular, or polyarticular, inflammatory attacks that quickly subside and do not necessarily leave crippling—by the presence of urate tophi, and by the peculiar changes seen near the ends of the bones in skiagraphs (Bruce's nodes). It is very generally regarded as a disorder of the uric acid metabolism which leads to the accumulation of excessive quantities of uric acid in the blood. The belief that gout is due to the presence of a poison circulating in the blood has been held since the days of the Roman Empire and the belief that this poison is uric acid has been held more than a hundred years. But uric acid is present in normal blood, and no definite confirmation by a reliable technique of the belief that there is a difference in the amount of uric acid in gouty and normal blood was forthcoming until as recently as the year 1912. The matter is not yet settled beyond dispute; undoubted cases of gout sometimes show normal and even low uric acid in the blood, and a high uric acid content of the blood is not infrequently found in persons with no evidence of gout. Various hypotheses as to the cause of the accumulation have been offered, the most widely accepted being that imperfect excretion through the kidneys is responsible.

Uric acid is an oxidation product of purin and, in

the body, comes only from the oxidation of other purin derivatives. A certain amount is derived from the oxidation of the purin compounds of the body tissue itself, a certain amount from the oxidation of purin compounds of the food. The purin compounds which occur in the body are chiefly four: adenin, guanin, xanthin and hypoxanthin—the last two, in turn, being probably derived from the first two—and these compounds occur chiefly in the nucleoprotein of the cell nuclei. The process of formation of purin compounds from nucleoproteins by digestion or hydrolysis is shown by the following scheme:



The following scheme shows the relation of these purin compounds to each other.




By successive processes of oxidation and hydrolysis the changes indicated by the arrows take place.

A certain amount of uric acid is, then, derived from the adenin and guanin in the nucleoproteins of the cell nuclei of the body itself even when no foods are taken; a certain amount, in addition, is derived from the adenin and guanin of the nucleoproteins of the cell nuclei of the food. From this it can be seen why foodstuffs rich in cell nuclei material—liver, pancreas, and other glandular organs—give rise to more uric acid than foodstuffs richer in interstitial tissue.

As already stated, the relation of uric acid to the etiology of gout is not yet settled, but, if we wish to give our patients the benefit of the doubt, we can employ measures to decrease the formation of uric acid in the body and measures to facilitate its excretion. To decrease the formation of uric acid, we restrict foodstuffs rich in purins—meat, fish, beans, peas, and oatmeal; organs like the liver, pancreas, and thymus which contains much nuclear material are especially rich in purin bodies. Tea and coffee contain caffein which is also a purin derivative. Eggs, milk, and vegetables—except beans, peas, and oatmeal—are relatively poor in purin compounds.

To increase the elimination of uric acid, lithium salts, various alkalies, and derivatives of piperazin have been extensively administered with the hope of forming salts of uric acid that are more soluble than the sodium salt found in the gouty tophi. This is a very irrational procedure; in such a case it is always the most insoluble salt that is formed, not the most soluble. A new drug, atophan, has recently been given to increase the elimination of uric acid; it appears to make the kidney more permeable to uric acid; but, besides being very un-

pleasant to take, it does not always ward off attacks.

As a matter of fact, gout is very difficult to treat successfully. The value of a purin-free diet has not been conclusively demonstrated; empirical methods sometimes give better results. The most diverse dietetic rules have been recommended; some physicians recommend cutting down carbohydrates, others decreasing proteins, others decreasing fats; some lay great stress on the ingestion of, or the abstinence from, certain special articles of diet. It is probable that the best diet in gout differs with different patients; cases are not infrequently reported in which the ingestion of a small amount of certain articles of food or drink is promptly followed by an attack of gout. The foodstuff responsible for the attack differs with different persons; often it is an alcoholic drink—a glass of port in one case, a glass of champagne in another; such substances are to be avoided by susceptible persons. Gouty patients should be abstemious in eating and drinking. Alcoholic drinks and meat should be much restricted; milk, fruit, and vegetables may be taken freely. Treatment at mineral springs is often attended with good results; probably not on account of the lithium or other mineral constituent of the water, but as a result of the large quantity of water taken, and the other details of the treatment. A certain amount of exercise is advisable; massage and stimulating baths are helpful. During acute attacks the joint should be wrapped up in a soft cotton protective bandage and the other measures recommended for the treatment of the affected joints in cases of acute rheumatic fever tried. Internally, salicylates and wine of colchicum are given. To

promote the excretion of waste products, the milder measures of stimulating the bowels, skin and kidneys used in cases of arteriosclerosis and nephritis are suitable.

The widely-spread, popular belief that uric acid is responsible, not only for gout, but also for a great group of other disorders is due practically entirely to the writings of an Englishman named Haig; it is based on vague and erroneous assumptions, false reasoning, and data obtained by faulty technique, and has no foundation whatever in what scientific investigators consider facts. The reasoning responsible for the belief runs somewhat as follows: (1) patients with gout frequently have many irregular, vague, and unusual symptoms referable to the gastro-intestinal tract, the nervous system, the lungs, skin, eyes, and other organs; and since (2) the joint symptoms of gout are due to uric acid; (3) these irregular manifestations of gout are due also to uric acid; (4) **therefore**, various irregular, vague, and unusual symptoms referable to the nervous system, lungs, gastro-intestinal tract, skin, eyes, and other organs in other patients, even those who do not show any of the recognizable signs of gout, are due to uric acid! With the increased knowledge and improvement in diagnostic skill less and less is heard about this so-called uric acid diathesis in the sense of Haig, the term, if used at all, being restricted to gout.

# OTHER CHRONIC DISEASES.

In the foregoing chapters the attempt has been made rather to establish a point of view than to convey detailed information regarding methods of treatment. The point of view emphasized throughout is that, in the treatment of chronic disease, our primary object is not to restore the anatomical integrity of diseased organs but to improve their efficiency. A sufficient number of the important diseases have been discussed to indicate how these principles are carried into practice. In other diseases the same general principles are borne in mind.

## Arthropathies.

Diseases of the joints are very difficult to discuss in a concise and satisfactory manner; on whatever phase of the subject we touch—etiology, classification, treatment—we find the greatest disagreement among investigators. Regarding the nature of the process in some of these conditions the widest differences in opinion are held; different writers may consider the same condition a nervous disease, an infectious disease, or a disease of metabolism. The terminology is so confusing that it is often difficult to tell what particular form of disease a writer may be discussing. To outline the general principles of treatment is not, therefore, a very simple matter.

We do recognize a distinct form of acute disease—acute rheumatic fever; the difficulties referred to are associated chiefly with the group of chronic arthropathies—those included under such terms as

rheumatoid arthritis, arthritis deformans, hypertrophic arthritis, chronic arthritis of the infectious type. The patients live a long time, often suffer great distress and pain, and their functional efficiency as a whole is often severely handicapped by deformities. In such conditions the necessity for a broad point of view regarding the purpose of treatment, and tolerance and sympathy for any suggestion which may improve the functional efficiency of the patient in any way is especially necessary. There are scarcely any conditions in the domain of chronic medicine where ingenuity and great patience on the part of physicians are more necessary than in chronic joint diseases; the whole realm of therapeutics is called upon; drugs—internally, and externally—hydrotherapy, active and passive motion, massage, diet, surgery, mechanical appliances, and psychotherapy, all have their place in the treatment of chronic arthropathies. The principles of the treatment of acute disease and of chronic disease both are used as a basis. The various subjective symptoms are, of course, treated directly as well. All the various methods of treatment come under one or more of these headings. To take only one example, namely, mechanical appliances: these may be employed to correct anatomical defects, as in the case of the various braces and plaster jackets used to correct spinal curvatures; to relieve strain, as in the case of the splints used to support fractured bones; or to improve function, as in the case of an artificial limb.

During acute stages when there is pain and tenderness the patient is kept at rest in bed. When there are no acute symptoms, as much exercise is

given as possible without strain or violence; this may take the form of active motion, passive motion, or massage. Great attention is given to mechanical methods of relieving tension and to supporting different parts of the body with straps, plasters, and bandages. Various surgical methods are used to correct deformities. Special forms of baths—baking in hot air, electric light baths—and passive congestion through the use of different kinds of bandages are very useful in relieving pain and promoting the nutrition of the joints. Many forms of treatment directed at possible etiological factors are tried. It is very generally agreed that some forms of chronic rheumatism have an infectious basis so that very complete physical examination is devoted to discovering sources of infection; the removal of foci of infection in the teeth, tonsils, and seminal vesicles is often followed by improvement. Vaccines are sometimes used. Gastro-intestinal putrefaction appears to be sometimes responsible for joint disease and the condition improves under dietetic treatment. It should not be forgotten that even in cases where the bacteria are not originally responsible for the joint trouble the weakened joint tissues may be more susceptible to the products of bacterial activity constantly being absorbed than are the tissues of normal joints. Recent writers have laid great stress on the significance of enteroptosis and faulty position of other parts of the body: it has been pointed out that a malposition in one part of the body is offset by a compensatory malposition of other parts, especially of the joints, leading to strain and pathological changes in the organs, and that attention to proper posture is often followed by im-

provement. In recent years observers have been pointing out that the incidence of certain forms of disease differs in persons of different anatomical types, and attempts are being made to make this the basis of therapeutic attack especially in joint diseases. It is suggested that different anatomical types correspond to different diathetic types and that these individual differences have to be taken into consideration in treatment. This is the basis of some of the forms of postural and dietetic treatment now under investigation. Certain forms of arthropathy are probably due to faulty metabolism and for this reason many special forms of dietetic treatment have been recommended.

Briefly, then, in the treatment of chronic joint disease the same general principles that are used in the treatment of other chronic diseases are employed; by rest of function, on the one hand, and stimulation of function, on the other, attempts are made to improve the general efficiency of the patient as a whole. In the preceding paragraphs the intention has been merely to outline very briefly the way in which these principles are applied; a more detailed discussion of the methods used in individual cases such as can be found in the special textbook on orthopedic surgery would be out of place at this point.

### Diseases of the Neuro-Muscular System.

The question of accurate diagnosis occupies so great a proportion of the attention that is devoted to disease of the nervous system that the student often hears little about treatment. Nevertheless, the same general principles of treatment as those used

in other chronic disease—rest and stimulation— are used in these diseases. In the more acute stages stress is laid especially on rest; in the chronic stages, on stimulation and exercise. In the acute stages of anterior poliomyelitis, locomotor ataxia, and hemiplegia, for example, the patient is kept at rest, bodily and mentally. In the chronic stages of these conditions the principles of treatment, namely, stimulation and exercise, depend on two factors: (1) Any affected muscle is under the influence of a number of different neurones and often not all the neurones are diseased; in such cases the various forms of stimulation and exercise serve to educate and train the intact neurones to do, in part, the work of the diseased neurones. (2) Complex movements are performed not by one set of muscles but by groups of muscles, and if one muscle of a group becomes paralyzed the other muscles of the group can often be trained to make up in part for this handicap. In other words, although we may not be able to restore the anatomical integrity of muscles or nerves that have been destroyed, the functional activity of the patient can sometimes be so greatly improved that we speak even of cures.

In acute conditions the patient is kept at rest. During the acute stage of hemiplegia, for example, the patient should be kept at rest in bed, and, if the blood pressure is high, as in arteriosclerosis, venesection should be done; if the hemiplegia is the result of an embolus, or thrombus (in heart disease or rheumatism, for example) and the pulse is weak, venesection may not be advisable. The bowels should be kept active—in an unconscious patient even drastics may be needed. An ice bag should be

kept on the patient's head; the diet should be light; the patient should be protected from bedsores. When the condition is the result of syphilis, potassium iodide may be given.

After convalescence is well established the various forms of exercise and stimulation should be instituted. To stimulate, we use active motion, passive motion, electricity, massage, and hydrotherapy. Various forms of active exercise have been worked out and described in the special textbooks. The Zander apparatus is adapted for the graded exercising of individual groups of muscles, but the same result can often be obtained by improvised household methods. In patients with less power in the muscles, massage and electricity can be used. In infantile paralysis, for example, the affected muscles should be rubbed, kneaded, and massaged with oil for months or years, if necessary, to maintain the nutrition of the muscles in order that, as the nervous control of the muscles improves, there will be well nourished muscles for the nervous system to act on. Since many diseases of the nervous system, bones, and joints are followed by disuse atrophy of the muscles, this principle should be borne in mind in any condition leading to decreased use of the muscles. Even in disease of the heart muscle the value of exercise should not be forgotten; it is a question if more attention should not be given, where it is possible, to graduated exercise of the heart. Stimulation of the skin stimulates the nervous system, and various forms of hydrotherapy which stimulate the skin may help the nutrition of the muscles. In locomotor ataxia, where there is a loss of the power of accurate control of muscular move-

ment, special exercises (Frankel's) aimed at gradual training in control are often followed by marked improvement. Many different devices are employed; usually the patient begins with some simple exercise and proceeds to gradually more complicated ones. A device very commonly employed is to require the patient to walk on a strip of carpet very slowly and accurately placing his feet on footprints outlined on the carpet.

More direct forms of treatment may be used to combat subjective symptoms, and to correct deformities. To combat pain, for example, rest in bed, baths, and the same local analgesics, counter irritants, and internal hypnotics used in other painful disturbances are used. In diseases such as poliomyelitis, accompanied by deformity, mechanical appliances may be used to correct the deformity. An example of still more direct form of treatment is the use of salvarsan in tabes.

### Other Conditions.

In the various forms of defective mentality great attention has been paid to the development of methods of measuring the degree of mental capacity, and to the establishment of institutions where patients with mental disease can be protected (rest) from the stress and strain of ordinary life and where especial attention can be devoted to their education (stimulation). Neurasthenics, for example, are believed to be persons whose capacity for standing severe nervous and mental strain is below normal—compare them with patients having heart disease, the efficiency of whose circulatory apparatus is below par; in treating neurasthenics, therefore, efforts

are made on the one hand to protect them from undue nervous and mental strain (rest), and, on the other hand, to improve their general nervous and mental efficiency (stimulation) so that they can stand greater demands.

In the treatment of skin diseases the rule is protection and soothing measures for acute or inflammatory conditions, stimulation for non-inflammatory conditions. In these cases of nervous, mental, and skin diseases we have again examples of the same principles of rest and exercise. But in these and other conditions the treatment becomes increasingly a matter of the details of applying the principles of rest and stimulation, and for these details the student naturally turns to the special textbooks and clinics.

# SPECIFIC INFECTIOUS DISEASES.

Although, as pointed out in the introduction, a close analysis shows that, theoretically, the same general principles are at the basis of treatment in both acute and chronic disease, the difference being merely in the degree of emphasis that is laid on different phases of treatment, these differences in emphasis are so great that for practical purposes it is simpler to regard the principles of treatment as different in the two cases; the aim of treatment in acute specific infections being complete removal of disease and complete restoration of the normal condition; the aim in chronic disease, to increase the functional efficiency to as high a plane as possible under the circumstances, and maintain it there. And it was pointed out, too, that the various methods of treating the specific infectious diseases and other acute diseases may be divided into three groups:

(1) methods of preventive medicine;

(2) treatment aimed directly at the cause of the disease;

(3) treatment aimed indirectly at the disease itself, directly at the various organs and the general metabolism.

Treatment aimed at the subjective symptoms may also be mentioned. Empirical tendencies will be combated and a more intelligent organization of the facts of therapeutics fostered if we regard the treatment of these specific infectious diseases not as something that is different for each individual disease, but as something that is the same in principle in all of them, showing differences merely in

the degree of emphasis which is placed on these different phases of treatment. In smallpox and scarlet fever, for example, **preventive medicine**, preventing the spread of the disease is much emphasized; in diphtheria, much reliance is placed on **direct** treatment with antitoxin; **indirect** treatment of the disease, treatment aimed more directly at the general metabolism and the various organs, is depended upon for results in pulmonary tuberculosis, typhoid fever, and pneumonia; and in acute rheumatic fever the intense pain calls for special attention to symptomatic treatment. It is these differences in the emphasis laid on different phases of the treatment that somewhat obscure the fact that the same general principles are used in the treatment of all the acute infectious diseases.

The details of the methods of **preventive medicine** cover a very wide range, the differences depending on etiology and mode of transmission. Some of these details—national quarantine for plague and yellow fever, mosquito extermination for malaria and yellow fever, vaccination for smallpox—belong rather to the department of hygiene than to therapeutics; others, such as those pertaining to the disposal of excretions and other details of the care of individual patients with typhoid fever, scarlet fever, and similar conditions, are usually discussed in textbooks of therapeutics. But these details need not be discussed here; their purpose and principles are easily understood.

A discussion of specific and other forms of **direct treatment**, important as they are, can also be dismissed with a few words. Such methods include not only treatment with specific antitoxins, but also

such treatment as the use of quinine in malaria; salvarsan, mercury, and potassium iodide in syphilis; surgical methods such as the removal of a diseased appendix, or evacuation of an abscess, and many other similar methods. In this category, too, may be properly included such methods as the administration of large quantities of water, the subcutaneous or intravenous injection of normal salt solution, the use of alcoholic drinks, stimulation of the kidneys, bowels and skin in persons with pneumonia, acute rheumatic fever and other specific infectious diseases, in the hope of diluting and combating the toxins and promoting their rapid elimination. The purpose and principles of treatment in all these cases are usually so clear that they do not call for further discussion here.

In most of the specific infectious diseases we still have no specific cure, and reliance must be placed on **indirect treatment.** In such cases the disease must be combated by the natural defenses of the body itself; our treatment is aimed, not at the disease, but at the patient, and is intended to aid him in increasing his power of combating the infection. The disease itself is left to run its course but under conditions which, so far as we can influence the conditions, we believe to be those which promote the maximum degree of efficiency of the various organs and of the general metabolism. In our ignorance of exactly what conditions are best for the patient, it is often a question if some of the methods we use do shorten the course of the disease or influence it in other ways; but we hope and believe that, on the whole, they increase the chances of recovery. The methods by which we try to bring about these ideal

conditions for the patient are similar to those used in the treatment of chronic disease; they are intended either to stimulate and improve the working power of the heart, the gastro-intestinal tract, the kidney, and other organs, and the general metabolism, or to rest and protect these organs, and the metabolism. Just as in the case of specific infectious diseases in general it was pointed out that it is better to regard the treatment not as fundamentally different in the different diseases but simply different in respect to the amount of emphasis which is laid on the various phases of the treatment, so, too, in the case of those specific infectious diseases which are not capable of direct specific treatment it is better to regard the treatment not as fundamentally different in the different diseases, but different only in the relative amount of attention given to the various parts of this phase of the treatment as a means of promoting the patient's resistance. In the protracted course of pulmonary tuberculosis, for example, much attention is given to that part of the general metabolism which has to do with methods of keeping the tissues in a high state of nutrition. In the case of pneumonia the disease lasts too short a time to lead to inanition; the question of nutrition is, therefore, a minor one compared with what it is in phthisis, but circulatory failure and other ill effects of the toxemia are much feared and attention is, therefore, given to methods of improving the heart and circulation and of combating the toxemia. In typhoid fever the duration of the disease is neither very long nor very short and the question of nutrition has therefore been a moot point—is the danger of inanition great enough so that it is necessary to risk the apparent dangers attached to a high diet?

In the treatment of specific infectious diseases the greatest attention on the whole is given to methods of influencing the general metabolism. The two chief problems are those connected with methods of increasing the strength of the patient by promoting his nutrition and those connected with methods of decreasing abnormally high temperature. It is not entirely clear yet whether or not there is a toxic destruction of tissue in specific infectious diseases, but, whether for this reason, or on account of lack of appetite, patients with such diseases lose weight and strength and it is often a problem how to maintain the nutrition. This matter is especially important as the duration of the disease increases. In the case of pulmonary tuberculosis, for example, the problem is largely one of keeping the patient well nourished. Patients with incipient or chronic pulmonary tuberculosis do best when kept out of doors in a cold, dry, stimulating climate and given as much food as they can digest without distress. A word of caution concerning overfeeding is needed; it has been observed, namely, that tuberculous patients sometimes do badly when the digestive system is overtaxed; it should be remembered that it is not the amount of food that is eaten that counts but the amount digested. Many physicians believe that alcoholic drinks in moderation have a place in the therapy of the specific infectious diseases. They point out that beer, wine and other alcoholic drinks which are very easily taken by the patient not only have a nutritive value in themselves nearly equal to that of fat, but, in stimulating the appetite and increasing, perhaps, the absorption, they improve the nutrition indirectly as well; they point out, furthermore, that the im-

provement in the subjective condition resulting from relief of dyspnoea, nausea and sleeplessness, and the euphoria brought about by alcoholic drinks in moderation are desirable in that such factors preserve the strength of the patient.

In the belief that high temperatures may lead to parenchymatous degeneration of various organs, it has been the common practice to try to keep down the high temperature. There is, however, a greater tendency in recent yars to attribute the damage to various vital organs seen in infectious diseases not so much to the high temperature as to the poisonous products of bacterial activity and, though it is still believed that temperatures of 105° or more may be responsible for parenchymatous degeneration, moderate fever is treated now chiefly on account of the unpleasant subjective symptoms for which it is responsible. The therapeutic measures in common use for reducing high temperature are directed at the general metabolism; they are (1) measures designed to decrease metabolic activity—(a) rest in bed, and (b) a low diet; and (2) methods to directly reduce the temperature—(a) hydrotherapeutic measures and (b) antipyretic drugs.

Rest in bed—complete muscular inactivity—it is everywhere agreed, helps keep down the temperature. Patients with fever are kept at rest in bed during the fever. In the case of pneumonia, typhoid fever, and similar diseases this means throughout the course of the disease; in the case of patients with chronic disease associated with acute exacerbations and rise of temperature, as in some cases of tuberculosis and endocarditis, for example, it means so long as the temperature remains above normal.

On the question of the kind of diet best suited to fever patients there has not been such unanimity of opinion; some clinicians have advocated a very low diet, others a very high diet. Those who believe in a low diet for fever patients have insisted that foodstuffs increase the metabolism and, therefore, raise the temperature. The advocates of a liberal diet for fever patients point out that such patients who are on a very low diet may lose much tissue—as much as 6 or 8 pounds of muscle—which is oxidized to provide fuel to maintain the high temperature, and that this loss may well decrease the resistance of the body; they believe that some of this body tissue may be spared by a liberal diet.

The discussion has been especially acute in the case of typhoid fever. In the case of tuberculosis the fever is so slight as a rule and the disease lasts so long that the question of nutrition overshadows all others; in the case of pneumonia the duration is so brief that starvation and loss of body tissue are not serious questions; in the case of typhoid fever both the high temperature and the question of inanition may be serious. Certain complicated scientific questions are involved, and it is, moreover, very difficult to settle the questions relating to the clinical results following the use of different diets. The clinical questions have not yet been definitely settled but some of the metabolic questions have been successfully attacked. It has been shown that the increased destruction of body tissue—in typhoid fever, at any rate—is probably not toxic but due to the decrease in foodstuffs, on the one hand, and the increased consumption of heat-producing material to maintain the high temperature, on the other;

and that the negative nitrogen balance and the presence of kreatin in the urine—another evidence of destruction of body tissue—which results from it, may be decreased by a liberal diet. One diet which has been recommended and carefully studied is made up chiefly of milk, cream, eggs, and lactose in the following proportions—1 to 2 liters of milk, 3 to 6 ounces of cream, 1 to 3 eggs, and a pound or more of lactose per day (lactose is not so sweet as cane sugar and can, therefore, be taken in larger quantities); this gives a diet containing 60 to 100 grams of protein, 120 to 250 grams of fat, and 500 or more grams of carbohydrate, and is equivalent to 3000 to 5000 calories of energy. Some clinicians give a more varied diet, adding even finely minced meat. Carbohydrates in abundance were chosen on account of their low specific dynamic effect; it has since been shown that there is no ground for fearing an increase in temperature from the specific dynamic effect of the food given; the specific dynamic effect seems not to be present in cases of fever. Why this should be so is not clear, but possibly the stimulation of the metabolism resulting from the ingestion of food is so small in comparison with the stimulating effects of the fever that it is not demonstrable.

Clinical observation shows that the general condition of the patient is better on a liberal diet; that the toxicity is lessened and convalescence hastened; that the patients lose less weight; and that the death rate is lower and hemorrhage and perforation less frequent. It is, of course, difficult to show that the improvement in the course of the disease or the better ultimate results are due to the

liberal diet; but since it has no effect in increasing the temperature and no other observable bad effect, it seems reasonable to suppose that it helps to fulfill one of the objects of treatment in acute disease, namely, that of promoting the strength of the patient. The favorable effect in pulmonary tuberculosis of combating the disease by feeding the patient up and improving the general nutrition while leaving the local condition to itself has long been recognized, but typhoid fever is the only acute infectious disease in which the effect of a liberal diet has been scientifically studied; it seems reasonable to suppose, however, that the conclusions reached should apply to other fevers accompanied by loss of tissue, and that the importance of a high diet in fever is, in a general way, proportional to the duration of the fever.

Hydrotherapeutic measures are much used to combat high temperature. Opinions differ regarding the advisability of baths when the temperature is not dangerously high; the question is one that can be gauged somewhat by the effect of the bath on the comfort of the patient—whether the effect on the toxemia and general condition is such that the patient feels better; or whether the good is more than offset by the bad effect of the turning, twisting, and moving about incidental to the bath. We now attribute the damage to parenchymatous organs which results from specific infectious disease rather to the toxin than to the temperature; but, on account of possible damage to the heart and other organs which may result from very high temperature, and on account of the good effect on the subjective symptoms and the toxemia, attempts are

made to keep the temperature from rising too high. The chilling of the skin dilates the superficial vessels, heat is lost more rapidly, and the temperature falls; as a result, the stupor lessens, the mind becomes clearer, insomnia becomes less troublesome; the effect on the heart, too, is good, and the mortality is probably decreased. It is now recognized, however, that the good effect of the baths lies not alone in the reduction of temperature but also in diminishing the toxemia and improving the general condition of the patient. Good results are observed when the temperature does not fall; in some cases, indeed, where it even rises after the bath; and there are clinicians who recommend hot baths instead of cold baths for fever. Various forms of hydrotherapy may be used; the patient may be placed in a bath at 80° to 90° and kept there twenty minutes or until it cools to about 75°; or cold sponge baths may be given. Cold packs are also used when prostration is great; the patient is wrapped round with a sheet wrung out in water at 50° to 65°. When milder measures are necessary, sponging with cold water or with alcohol is used. In old persons or others with a heart that is at all weak, cold baths are contraindicated.

The poisonous and depressant antipyretic drugs are sometimes used to lower high temperature, but general opinion is against their use and they are much less used now than formerly. The cause of the increase in temperature in infectious diseases is not entirely understood but it is probably due to an increase in irritability in heat dissipation, and a loss of the normal balance between heat formation and heat dissipation such that equilibrium is reached

on a higher level. The action of the antipyretics is believed to be due to their depressant action on the central nervous system, to the fact that they depress the center of temperature regulation as well as other centers. They do not lower the temperature when it is normal but, like other narcotics, act best on a center—like the heart center in fever—which is in a condition of persistent over-excitability. Antipyretic drugs are sometimes used by physicians in their private practice in cases where conditions are such that hydrotherapeutic measures are difficult to carry out.

It has been very generally believed that the commonest cause of death in pneumonia, typhoid fever, diphtheria, and many other acute infectious diseases is cardiac asthenia; and upon this belief has been based the common practice of stimulating the heart in these conditions. Recent investigations seem to indicate that in pneumonia and diphtheria, at any rate—the conditions which have been most studied—the circulatory failure may not be due so much to changes in the heart itself as to changes in the smaller arteries and capillaries. Whether these studies will lead to great changes in the therapeutics of these diseases is still uncertain; there has always been much difference of opinion on the question of when and how to improve circulatory function in acute infectious diseases—the use of drugs of the digitalis group in pneumonia is an example of such treatment. To combat heart weakness in elderly persons or others known to have a weak heart in cases of pneumonia, digitalis may be given from the beginning; to other pneumonia patients digitalis may be given as soon as the heart

shows signs of weakness. In anticipation of the strain that is believed to come on the heart at the time of the crisis, some physicians give digitalis in all cases after the third or fourth day. Strophanthus, strychnine, camphor, and aromatic spirits of ammonia are also used to stimulate the heart. When quick action is imperative, intravenous injections of strophanthus are used. In full-blooded persons with high, bounding pulse, and marked dsypnoea, venesection may help relieve the heart of undue strain. In the fevers of longer duration—typhoid fever, for example—cold baths are more relied on to stimulate the heart. It is said that a brisk purgation may sometimes avert a threatened attack of heart failure in cases of scarlet fever and certain other acute fevers. During convalescence from long-continued fever great care should be taken to increase only very slowly the strain on the heart. It is said that heart disease occurs more frequently as a sequel of acute infectious disease in those patients who are allowed to get up too soon.

Just as treatment may sometimes be directed at the heart in specific infectious diseases, so, too, it may be directed at the kidneys, gastro-intestinal tract, lungs, or other organs; a full discussion of the many details need not be carried out here. The purpose and principles of the details will easily be understood in the light of what has been said about the treatment of the chronic diseases of these organs.

Finally, for completeness, may be mentioned the treatment which is directed at keeping the mouth clean; treatment intended to prevent bedsores, and accidents resulting from delirium; and symptomatic treatment—all easily understood.